

**Strategic Considerations for
Support of Humans in Space
and
Moon/Mars Exploration Missions**

Life Sciences Research and Technology Programs

VOLUME I

**NASA Advisory Council
Aerospace Medicine Advisory Committee**

June 1992

ACKNOWLEDGEMENTS

The NASA Aerospace Medicine Advisory Committee (AMAC) wishes to express sincere appreciation for the efforts of all those who participated in the development of this report, "Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions." The Committee would like to single out the contributions of Dr. Arnauld Nicogossian for his foresight and wherewithal to initiate this prescient effort and his dedication and enthusiasm to see it through completion; the hard work of the Life Sciences Division staff to help put it all together; the commitment of the AMAC Executive Steering Committee to review, revise and evaluate all the critical questions; the individual efforts of the report chapter chairmen, Dr. Cary Mitchell, Dr. Reginald Edgerton, Dr. Robert Moser, and Dr. Richard Young; and the support and encouragement from the NAC to proceed with this important undertaking.

The Committee would also like to thank the writing committee members, especially Dr. John A. Rummel, Dr. Joan Vernikos, Dr. Donald Stewart, and Dr. Fran Haddy. AMAC also wishes to express special appreciation for the participation of the representatives from the NASA Program Offices including Space Station, Space Shuttle, Technology, and Exploration.

The ability to define critical life sciences priorities for pursuing the goal of human exploration is a major accomplishment. This effort would not have occurred without the totally committed contributions of Dr. Larry Biever and Dr. Lauren Leveton. The AMAC must express special thanks to these two fine professionals. Further the AMAC commends the efforts of all involved in making such a significant contribution to the U.S. space program. AMAC is confident that the findings and recommendations, along with the comprehensive data base will provide a strong foundation to plan our future exploration missions. We know what we have to do!



National Aeronautics and
Space Administration

Washington, D.C.
20546

Reply to Attn of:

Mr. Caleb B. Hurtt
Chairman, NAC
272 West Meadow Drive
Vail, CO 81657

JUN 03 1992

Dear K:

On behalf of AMAC, I am pleased to provide to you the enclosed report , "Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions." In the process of developing this report, AMAC deliberated with many individuals, including NASA program and project managers, scientists, and engineers, various advisory committees, and our Russian space partners. It represents a consensus among a diversity of perspectives regarding the life sciences research priorities.

This is a unique report in that it provides both a top-down and "grass roots" consensus of the internal and external life sciences communities. It is built upon a comprehensive database that serves to organize the major enabling research thrusts, integrates ground-based programs with flight resources, and provides a basis for identifying the national and international organizations and resources that must be brought to bear if we are to achieve our goal of space exploration.

The most salient finding based on a detailed analysis of all the scientific information available is, "there is no issue, *a priori*, that precludes human exploration to the Moon or Mars, if appropriately focused research is conducted and enabling technologies developed." Three major problems that must be the major focus of the biomedical life sciences program to support exploration are identified in Recommendation 1.

The AMAC will work with all elements of NASA to integrate the findings and recommendations of the report with the planning for future space missions, including the Space Station Freedom, the lunar outpost, and the mission to Mars. The report will be updated and refined as NASA plans and programs are further developed.

The efforts of the Life Sciences Division staff to create and consolidate the supporting scientific database for this report are to be commended. This database is unique in this nature and more detailed than anything produced by other science disciplines. It is a demonstration of the life sciences' intent to proceed with implementation of these strategic considerations for human space flight missions.

Mr. Caleb B. Hurtt
June 1, 1992

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This report comes at a time when detailed analysis of program priorities for exploration missions can play a critical role in defining the requirements and setting the pace for future space activities. It has been a tremendous opportunity to work together with so many individuals and develop a consensus of life sciences research priorities. I am pleased to turn the report over to you and the NAC.

Sincerely,



Harry C. Holloway, M.D.
Deputy Dean

Enclosure



National Aeronautics and
Space Administration

Washington, D.C.
20546

Reply to Attn of:

Dr. Harry C. Holloway
Uniformed Services University of
Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814-4799

JUN 03 1992

Dear Harry:

You and the AMAC are to be commended for your efforts to produce such an important, useful, and timely document, "Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions." You have put forth a strong, sound and reasonable strategy for setting life sciences research priorities and making decisions that will enable human exploration missions.

The report demonstrates a thorough understanding of the resources that are required if we are to meet the challenge of human space exploration. A broad, far-reaching, and integrated plan has been developed to guide the Nation's scientists, engineers, mission planners and policy makers in their decisions and commitments to the expansion of our knowledge in space life sciences.

On behalf of the NAC, I want to express congratulations to you, the AMAC, and the Life Sciences staff for their significant efforts in planning our nation's human exploration missions. I am confident that the findings and recommendations contained in this report will provide a solid foundation for our future space missions.

Sincerely,

Caleb B. Hurtt
Chairman, NAC



National Aeronautics and
Space Administration

Washington, D.C.
20546

Reply to Attn of:

Mr. Daniel S. Goldin
Administrator
Code A
NASA Headquarters
Washington, DC 20546

JUN 03 1992

Dear Dan:

I am pleased to forward with this letter the report of the NASA Advisory Council's Aerospace Medicine Advisory Committee. The report, "Strategic Considerations for Support of Humans in Space and Moon/Mars Missions," is the product of an intensive study by the AMAC, with participation from many NASA program managers, project scientists and engineers, advisory committees, and international science community. It represents an integrated consensus for establishing life sciences research priorities and making decisions that will enable human exploration missions.

This report is a template that will guide NASA scientists, mission planners and policy makers in their decisions and commitments to the expansion of our knowledge in space life sciences. It is based on an extensive database that serves to organize the major enabling research thrusts, integrates ground-based programs with flight resources, and provides a basis for identifying the national and international organizations and resources that must be brought to bear if we are to achieve our goal of space exploration.

The AMAC analysis concluded that within the confines of our current knowledge, there was no issue a priori that precludes human exploration of the Moon or Mars if appropriately focused research is conducted and enabling technologies are developed. AMAC did conclude that the three primary areas for research and technology development are: characterizing and alleviating risks from radiation, long-duration exposure to microgravity, and reliable life support systems. The AMAC analysis produced 15 findings and recommendations that either were considered "overarching" in that they affected fundamental policies concerning research and technology needs, or were categorized into one of three major thrusts: Environmental Health and Life Support Systems; Countermeasure Systems; or Medical Care Systems. The report also provides the resource requirements and milestones for life sciences deliverables.

To accomplish the strategic considerations set forth in this report, NAC strongly recommends a single focus of responsibility and accountability, within the NASA top management, for carrying out all agency life sciences/life support activities. The most effective structural solution for such focus is best decided by the agency

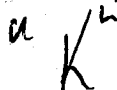
Mr. Daniel S. Goldin
June 1, 1992

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following review of previous committee recommendations and inputs from the Life Sciences community.

In conclusion, the report provides a strong foundation for planning our future space missions, it represents a consensus for setting life sciences research priorities, and it offers an integrated plan for making decisions to enable exploration missions. It is a high water mark for planning the respective programs for the future. Harry Holloway and his committee members, as well as the Life Sciences Division staff and other participants have made a significant contribution to the future of the nation's space program. It is a job well done.

Sincerely,

A handwritten signature in dark ink, appearing to be 'C. Hurtt' or similar, written in a cursive style.

Caleb Hurtt, NAC Chairman

Enclosures

PREFACE

The Augustine Committee developed an exciting, challenging blueprint for the future of the United States space program. They postulated that NASA has five space related operational missions: Space Science; Mission to Planet Earth; Space Utilization (goods and services made available for use on Earth); Transportation (economically reliable delivery of payloads to orbit); and Mission from Planet Earth, which culminates with President Bush's Space Exploration Initiative.

NASA also has a sixth mission, implicit in the Space Act, to develop the technology base required to assure continued American preeminence in space for the overall benefit of the nation. The debate over mission priorities, timing, and the size of the NASA budget continues within both the Administration and Congress. While it is still not clear which goals will be embraced now and in the future, whatever the choices, the nation should have the capability to execute the options chosen within predictable cost and schedule estimates.

Key to that capability will be the research and advanced technology data base that is available in the technologies critical to the chosen missions. However, over the past 20 years, NASA's investment in advanced space research and technology has been inadequate. Today's technology base is inadequate to support advanced space missions. It should be obvious that a modest increased investment in basic technologies today can reap major savings in future costs and schedules. But the program remains underfunded, at approximately two percent of the NASA budget, by a factor of nearly three.¹

By far, the biggest challenge postulated for NASA is Mission from Planet Earth, the focus of human activity in space, culminating with permanent presence on the Moon and landings on Mars. The President proposes, Congress opposes. But the question is not really whether we, either as a nation or a planet, will make the journey. The question is when.

We should use whatever time is available before a decision to proceed is made, to reduce fundamental uncertainties and assure that enabling technologies are ready for development. For the Moon/Mars exploration missions three areas predominate — propulsion, power, and support for humans in space.

This AMAC report, now fully endorsed by the NASA Advisory Council, is a milestone in the history of human space flight. Concluding that there is no issue that precludes human exploration of Mars, it defines a focused research and technology program to address the risks of radiation, long-duration exposure to microgravity, and reliable life support systems.

Footnote 1. The Report of the Advisory Committee on the Future of the U.S. Space Program (1990) and the National Research Council Report (1987), "Space Technology to Meet Future Needs."

This report "Strategic Considerations for Support of Humans in Space and Moon/Mars Exploration Missions," is intended to serve as a template to guide scientists, engineers, mission planners, and policy makers in their decisions and commitments to the expansion of our knowledge in space life sciences. It develops a strong strategy for setting life sciences research priorities and making decisions that will enable human exploration missions. It is a blueprint for our future exploration in space and the challenges that NASA, other agencies, and our international partners will face as we begin this new era of exploration.

The report is organized into six sections. Section I provides the Executive Summary and contains the 15 findings and recommendations. The recommendations are presented as follows: *Overarching Recommendations* (Recommendations 1 - 11); *Environmental Health and Life Support* recommendations (Recommendation 12); *Countermeasures Systems* recommendations (Recommendations 13 & 14); and *Medical Care Systems* recommendation (Recommendation 15). In addition, the Overarching Recommendations are further categorized according to ground, flight, or both types of activities. Section II identifies resource requirements and milestones for deliverables necessary to accomplish the research required to support human exploration mission solutions described in Sections IV, V, & VI that address the research thrusts (i.e., Environmental Health and Life Support Systems, Countermeasures Systems, and Medical Care Systems). For each thrust, the constrained and robust program is described. The constrained program included those elements defined as essential and critical — "criticality 1 & 2"), and the robust program included elements of all four criticalities — "criticalities 1, 2, 3, & 4." Section III addresses the Mission From Planet Earth goal, specifically, "to maximize scientific return from exploration that will benefit the people on Earth."

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I. EXECUTIVE SUMMARY

During the next several decades our nation will embark on human exploration in space. In the microgravity environment we will learn how human physiology responds to the absence of gravity and what procedures and systems are required to maintain health and performance. As the human experience is extended for longer periods in low Earth orbit, we will also be exploring space robotically. Robotic precursor missions, to learn more about the lunar and martian environments will be conducted so that we can send crews to these planetary surfaces to further explore and conduct scientific investigations that include examining the very processes of life itself.

Human exploration in space requires the ability to maintain crew health and performance in spacecraft, during extravehicular activities, on planetary surfaces, and upon return to Earth. This goal can only be achieved through focused research and technological developments. This report provides the basis for setting research priorities and making decisions to enable human exploration missions (Table I-1).

**TABLE I-1
MISSION SCENARIO¹**

MOON

- Visit (IOC)*
 - Timeframe: 2003-2006
accelerated date 2000
 - Surface: 14 days
 - Crew Size: 6
- Outpost**
 - Timeframe: 2007-2010
 - Surface: 40-180 days
 - Crew Size: 6
- Settlement**
 - Timeframe: 2007-2011
 - Duration: 360-600 days
 - Crew Size: 6-18

MARS

- Visit (IOC)*
 - Timeframe: 2014-2018
 - Duration: 600-1000 days
 - Surface: 30-100 days
 - Crew Size: 6
- Outpost
 - Timeframe: 2016-2020
 - Duration: 1500 days
 - Surface: 600 days
 - Crew Size: 6
- Settlement
 - Evolving capability

* Initial Operational Capability

** Mars Simulation would include 120 to 460-day Moon orbit

The report expands the recommendations of several previous advisory committees (Table I-2). It is based on the results of comprehensive studies conducted by 12 Life Sciences Discipline Working Groups (DWGs). The appendices (Section VII) contain the methodology and membership for this report. In conjunction with NASA scientists, the DWGs defined the unresolved issues considered critical to advancement of knowledge in their discipline.

Footnote 1. This report is based on current life sciences knowledge bases, Vision 21, The NASA Strategic Plan (1992) and Offices of Aeronautics and Space Technology, and Exploration planning (Appendix G). Table 1 is not based on any single specific mission architecture.

Table I-2 Recommended Life Sciences Milestones

LIFE SCIENCES CAPABILITIES TO SUPPORT EXPLORATION MISSIONS	AMAC REPT (SEE APPENDIX G)	SEI DATA BOOK (OAST) (SEE APPENDIX G)	NRC REPT (SEE APPENDIX G)	AUGUSTINE REPT (SEE APPENDIX G)	SYNTHESIS REPT (SEE APPENDIX G)	NASA HEI 90-DAY REPT (SEE APPENDIX G)	ROBBINS REPT (SEE APPENDIX G)	LIFE SCI STRATEGIC PLAN (SEE APPENDIX G)
1. ENHANCED RESEARCH AND ANALYSIS PROGRAM	X	X	X	—	X	X	X	X
2. RADIATION HEALTH DATA COLLECTION USING FREE FLYERS	X	X	X	—	—	X	X	X
3. COUNTERMEASURES FOR EXTENDED HUMAN-TENDED SSF CAPABILITY	X	—	X	—	—	—	X	X
4. HUMAN FACTORS GROUND SIMULATORS	X	X	X	—	—	X	X	X
5. HUMAN-RATED CELSS GROUND TESTBED	X	X	X	X	X	—	X	X
6. LIFE SCIENCES SSF TESTBED	X	X	X	X	X	X	X	X
7. MOON DATA REQUIREMENTS	X	X	—	—	—	X	X	X
8. LIFE SCIENCES STANDARDS AND REQUIREMENTS FOR MOON MISSIONS	X	X	—	X	X	X	X	X
9. MOON SCIENCE OPERATIONS	X	X	—	X	X	X	X	X
10. MARS DATA REQUIREMENTS	X	X	—	X	X	X	X	X
11. LIFE SCIENCES STANDARDS AND REQUIREMENTS FOR MARS MISSIONS	X	X	—	X	X	X	X	X
12. MARS SCIENCE OPERATIONS	X	X	—	X	X	X	X	X

An Executive Steering Committee, composed of members from the Aerospace Medicine Advisory Committee (AMAC) and Chairpersons of the DWGs, and other distinguished advisors initially prioritized those issues into three major research thrusts (Figure I-1) that enable missions to Moon and Mars. Finally, the full AMAC reviewed and prioritized the critical issues for this report (Table I-3). The report describes constrained and robust programs. The constrained program was defined as essential and contained criticality 1 and 2 elements; and the robust program included 1, 2, 3, and 4 criticalities. The constrained program contains those elements necessary for all human missions, but it may not be sufficient for Mars mission execution.

From its review, AMAC concludes that, within the current confines of our knowledge, no issue, a priori, precludes human exploration of the Moon or Mars if appropriately focused research is conducted and enabling technologies are developed. However, experimentation and/or long-term experience in space may disclose unexpected difficulties that will require reassessment of this conclusion.

The AMAC analysis identified 15 major issues (i.e., findings) and provides recommendations for corrective action. These findings and recommendations either were considered "overarching," in that they affected fundamental policies concerning research and technology needs, or were categorized into one of the three major research thrusts: (1) Environmental Health and Life Support Systems (EHLSS), (2) Countermeasures Systems (CS), or (3) Medical Care Systems (MCS).

Figure I-1 Life Sciences Research Thrusts

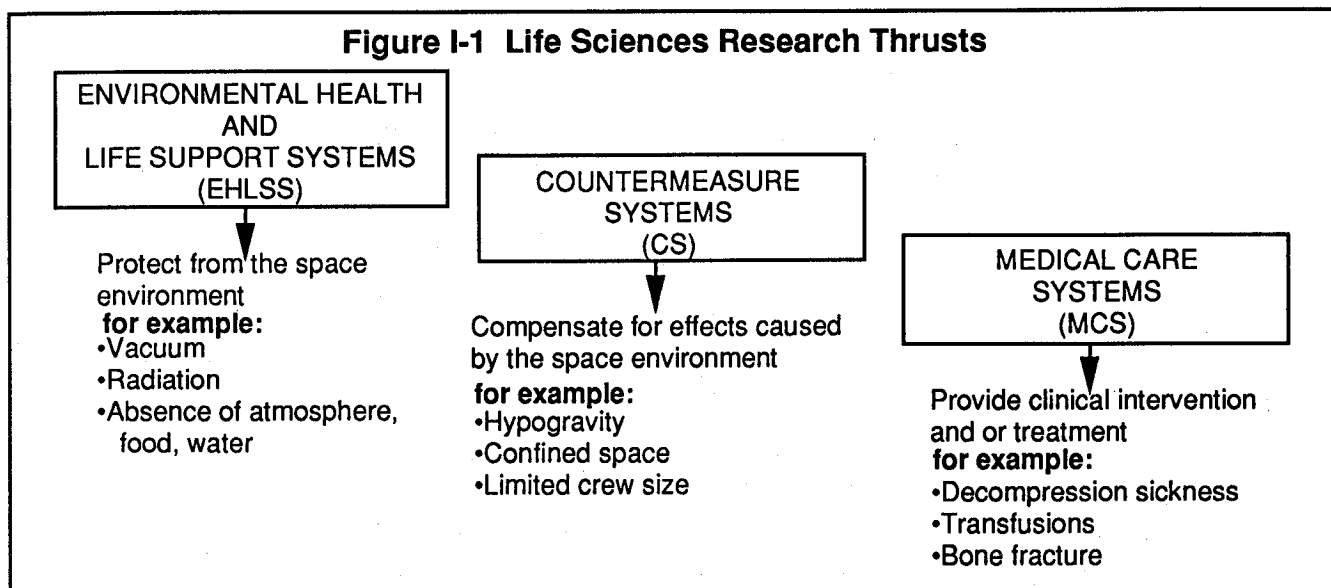


Table I-3 Definitions of Criticality

CATEGORY	PROGRAM	CRITICALITY			
		1	2	3	4
EHLSS	CONSTRAINED				
	ROBUST				
CS	CONSTRAINED				
	ROBUST				
MCS	CONSTRAINED				
	ROBUST				

Criticality Criteria

Criticality 1: Consensus that answer is required for Mars mission (known effect and known problem for mission).*

Criticality 2: Answers might be required, but science basis to evaluate risk is not adequate.

Criticality 3: Required for practical optimization of resources (or countermeasure effectiveness) and minimization of risk.

Criticality 4: Important science that is relevant to exploration mission.

*Crewmembers must be able to effectively perform mission tasks in transit vehicles and on planetary surfaces; and must recover, in a reasonable time, upon return to earth.

Category Definitions

Environmental Health and Life Support Systems (EHLSS) are designed to protect the crew from inhospitable space and planetary environments.

Countermeasure Systems (CS) are designed to continuously compensate for detrimental physical, physiological and behavioral manifestations of the space environment (e.g., microgravity, confined volume). They must provide acceptable mission performance and postflight recovery when: (1) EHLSS designed to provide habitable environmental conditions for the crew are not totally feasible because of mission design, or inadequacy of scientific or technological basis, or where cost and schedule are prohibitive; or (2) partial EHLSS failures occur, until appropriate remedial action is taken.

Medical Care Systems (MCS) are designed to handle illness and injuries based on probability of occurrence, to restore crew health for continued mission performance, or stabilize an ill or injured crewmember for rescue. MCS are also designed to handle illness or injuries resulting from temporary failure, degradation, or maintenance of EHLSS or CS systems, until full function is restored.

ENABLED SCIENCE		EXPLORATION CRITICALITY NOT APPLICABLE	
BASIC SCIENCE			

OVERARCHING RECOMMENDATIONS

To accomplish this recommended work, a single focus of responsibility and accountability, within the NASA top management, for carrying out all agency life sciences/life support activities is required. The 15 findings and recommendations are as follows:

Finding 1: Health risks from exposure to ionizing radiation, long-duration exposure to microgravity, and reliable, self-sufficient life support systems are the three major unresolved issues for human exploration.

Recommendation 1: Research and advanced technology development must focus intensely on characterizing and alleviating risks from radiation, long-duration exposure to microgravity, and development of life support technology. This effort must include continuing availability of a ground facility for proton and heavy charged particle (HZE) radiation research, variable gravity centrifuges on space-based platforms, and ground and space-based testbeds for life support systems.

Finding 2: In spite of numerous recommendations by previous committees, life sciences/life support efforts have not been funded or supported as a sustained and integrated program of research and technology development that will adequately support Moon/Mars missions.

Recommendation 2: Starting with the FY 1994 budget, provide sustained support for a phased and integrated program that includes Spacelabs, international flight platforms, and utilization of Space Station Freedom (SSF) early in man-tended capability (MTC). Accelerate availability of permanently man-tended capability (PMC) to develop, test and validate concepts for Moon and Mars missions, including as a minimum limited bioregenerative life support. Employ Moon bases when available to enhance the scientific database and develop, test and validate concepts, hardware and operational protocols for Mars surface operations.

Finding 3: Robotic precursor missions are required to prevent contamination of Mars or potential back-contamination to Earth, as well as to collect essential information necessary for radiation protection and development of life support systems.

Recommendation 3: Implement robotic precursor missions with life sciences participation to characterize radiation and resources available for life support, and for designing planetary protection protocols (i.e., contamination of Mars and back-contamination to Earth).

GROUND-BASED ACTIVITIES

Finding 4: Archiving and frequent updating of a comprehensive life sciences/life support database do not exist.

Recommendation 4: Based on the benchmark database generated during this study, develop a life sciences/life support database by FY 1993, and update it on a regular basis. Incorporate ground and flight-based mission results, relevant science and technology data from other NASA organizations, and evolving exploration scenarios and plans. Include appropriate information from other federal agencies, international partners, industry and universities. Mandate an annual AMAC review to assess progress toward answering critical questions defined in this plan.

Finding 5: Human exploration missions require fully coordinated and integrated participation among international, interagency, university and industrial institutions.

Recommendation 5: Achieve participation and full coordination of required international, interagency, university and industrial organizations by FY 1994.

Finding 6: Life sciences research in space has produced significant benefits to quality of life on Earth; additional contributions to human welfare on Earth can be expected from enhanced knowledge of the effects of gravity on biological systems, as well as from new medical and life support technologies developed during research to enable Moon and Mars missions.

Recommendation 6: Establish a regular AMAC evaluation of potential near- and long-term beneficial applications on Earth from life sciences research and technology development conducted for human exploration missions; promote further development and transfer of these applications to academia and industry.

Finding 7: National and international analog and testbed facilities (e.g., special facilities at NASA centers, DOD, DOE, NIH, National Science Foundation, and NOAA) for advanced space missions are unused or underutilized.

Recommendation 7: In concert with other agencies (e.g., DOE, NIH, NSF, NOAA, DOD), NASA must increase investment at NASA centers, universities and in industry to maintain and optimally utilize testbed facilities, particularly to promote research and advanced technology development.

Finding 8: Policies, equipment and procedures for preventing the back contamination of Earth and the biological contamination of Mars by humans are not yet developed.

Recommendation 8: Establish an interagency/international committee to focus development of planetary protection policy and appropriately fund the development of necessary equipment and procedures.

GROUND AND FLIGHT ACTIVITIES

Finding 9: Environmental Health and Life Support Systems, Countermeasure Systems, Medical Care Systems, and ultimately, mission design and hardware requirements, are driven by standards (e.g., air, water, and food purity) based on life sciences research and available technology. There is no comprehensive validated set of standards for Moon and Mars missions.

Recommendation 9: Establish an interagency coordinating task force to develop a comprehensive set of standards required for human exploration missions; jointly conduct a detailed evaluation of the adequacy of each item; and expand the existing programs to collect relevant data and reach policy decisions.

FLIGHT ACTIVITIES

Finding 10: The absence of SSF funding for basic biological and biomedical research (like BMAC) in space, will result in underutilization of this facility for both science and space exploration.

Recommendation 10: Enhance utilization of Shuttle middeck, Spacelab, and Russian assets for life sciences/life support, including BMAC, and provide early life sciences access for SSF. Immediately allocate resources for basic and applied life sciences research to facilitate utilization of SSF throughout the first 10 years of operations.

Finding 11: The current plan for a program in space life sciences and in the science needed for human exploration is well-balanced and must be supported. Partial funding of the program is likely to deprive NASA of a significant portion of the life sciences community.

Recommendation 11: Maintain a balanced, synergistic core life sciences program which provides additional resources necessary to enable Moon and Mars missions, define and support exobiology research on those missions, transmit knowledge to life sciences students and make such knowledge and technology available to private commercial enterprises.

ENVIRONMENTAL HEALTH AND LIFE SUPPORT SYSTEMS RECOMMENDATIONS

Finding 12: A high degree of self-sufficiency and reliability in the life support systems is required for exploration missions. Regenerative physico-chemical life support systems and hybrid bioregenerative life support systems are not adequately supported.

Recommendation 12: Accelerate efforts to enable trade-off studies of the life support system capabilities for any given exploration mission scenario.

Develop bioregenerative life support systems and associated testbeds on the ground and for SSF on a schedule and with a level of effort sufficient to support early Moon and Mars missions until physico-chemical capabilities are verified. Develop Controlled Ecological Life Support Systems (CELSS) for Moon and Mars bases.

COUNTERMEASURE SYSTEMS RECOMMENDATIONS

Finding 13: Full characterization of the human adaptation process to long-duration space flight is incomplete. Differentiation between healthy adaptation and pathophysiological adaptation is required in order to devise appropriate countermeasures.

Recommendation 13: Develop a prospective standardized health and performance monitoring capability and research program to be implemented on all national and international missions, thus creating a consistent database to assess the efficacy of countermeasures. This database would also include information on environmental conditions and habitability factors (e.g., human-machine interfaces) associated with this research.

Finding 14: Ultimately crew selection, organization and training will be a critical countermeasure for dealing with psychological and physiological problems associated with space travel.

Recommendation 14: Using the databases created by the life sciences research program in analog and space flight environments, develop and test protocols for crew selection, organization and training.

MEDICAL CARE SYSTEMS RECOMMENDATIONS

Finding 15: Experience with medical care in space is limited to first generation systems appropriate for short-duration missions (i.e., essentially enhanced first-aid kits). Data and techniques to define equipment requirements and protocols appropriate for transit vehicles and planetary habitats are not available. Experience with decompression sickness in space is equally limited.

Recommendation 15: Develop clear protocols for medical triage and treatment of surgical and medical problems during transit and on planetary surfaces. Conduct multidimensional trade-off studies between risk for specific medical events, medical care system equipment and capabilities and crew medical skills, versus telemedicine and rescue capabilities. Develop and test health maintenance systems in ground-based simulators and at remote sites and deploy them to SSF for space flight validation. Evaluate effectiveness of the hyperbaric chamber on SSF.

In addition to the specific issues and recommendations, the AMAC analysis emphasized the benefits of providing access to space for life sciences basic research.

Space flight provides the only environment in which the force of gravity can be partially or completely removed to permit assessment of the undoubtedly profound influence of gravity on the structure and functional evolution of all living organisms.

AMAC realizes that a time table for space exploration has not been established and recognizes that development may occur in the future that will alter the emphasis, importance and timing of these findings and recommendations. Further, the ultimate time of transit to Mars is uncertain because of the undetermined nature of the propulsion scheme to be employed.

Despite these uncertainties, AMAC believes the findings and recommendations reflect the best assessment, that can be made at this time, of the most important issues in the life sciences facing human exploration, and would apply independent of mission scenario. Indeed, most of the issues identified and the paths proposed examine basic questions concerning the possibility of an extraterrestrial venture and are at the heart of any determination as to the potential of such missions.

AMAC did not presume to undertake the task of NASA program planning. However, it felt a responsibility to determine whether the recommendations could be implemented in a timely manner consistent with NASA's published plans. Figures 1-2,3, and 4 identify life sciences milestones consistent with the plans available in NASA (e.g., Vision 21— The NASA Strategic Plan, January 1992, and Office of Aeronautics Space Technology Plan provided on September 23, 1991). Figure 1-5 illustrates major opportunities for continuous support for external science group input to development of hardware and the definition of the science included in the Moon and Mars missions. External science community will be involved in defining the major life sciences research areas, lunar precursor missions, the research on the lunar base, Mars precursor missions, and the research in the Mars transit vehicle and for the Mars base. Detailed schedules and specific milestones and deliverables for human exploration missions are provided in Section II of the report. The science and technology necessary to provide the deliverables is discussed in Sections IV through VI. Section III addresses the Mission From Planet Earth goal: "to maximize scientific return from exploration that will benefit the people on Earth." This section discusses three categories of research:

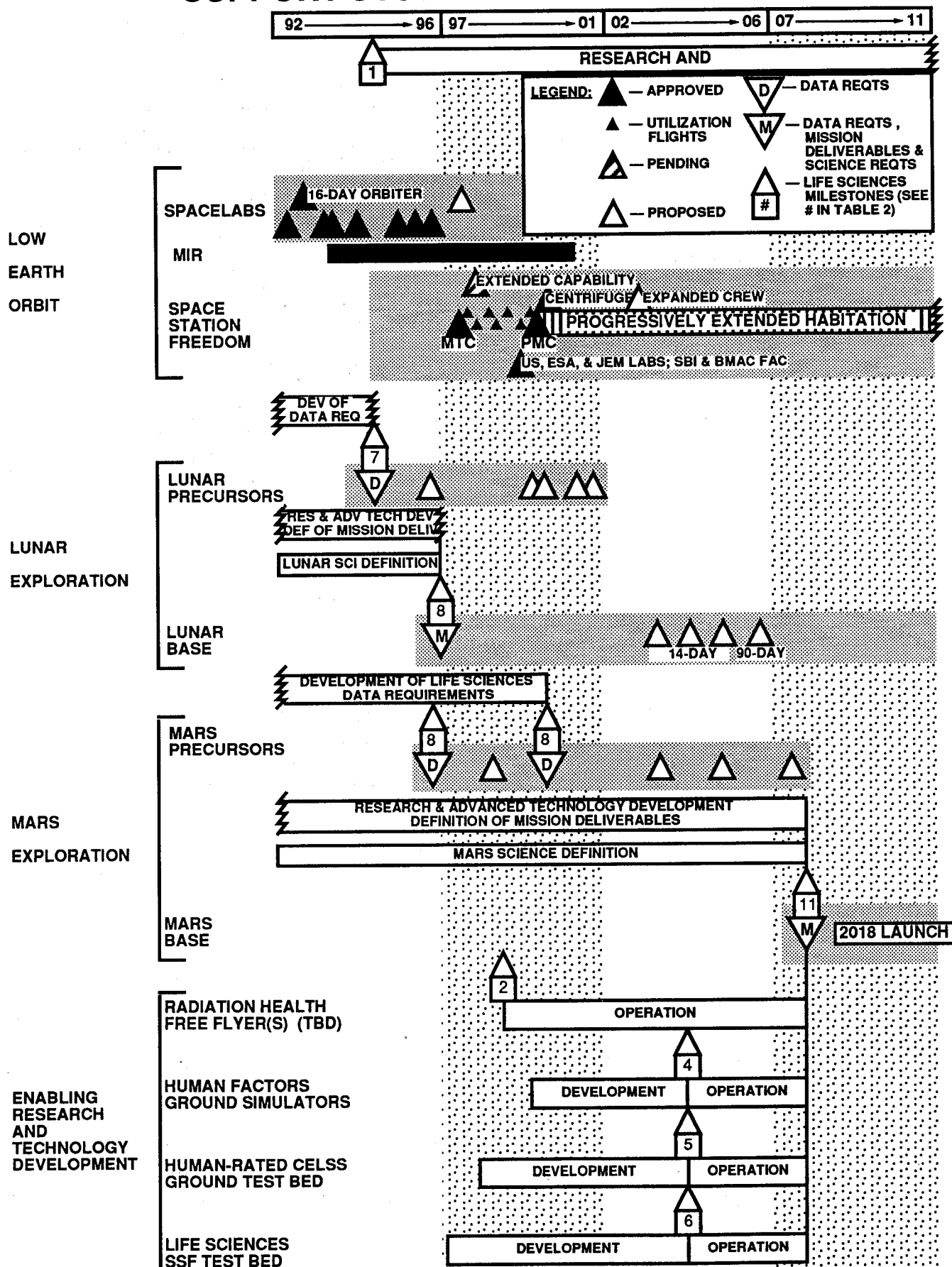
- Science identified as supporting MFPE that is justifiable based on its inherent scientific or technical merit.
- Science that is enabled by Moon and/or Mars exploration missions.² Enabled science is a unique component of basic science.
- Basic science not directly applicable to Moon or Mars missions.³

Footnote 2. 12% of the critical questions in Life Sciences Discipline Plans will be specifically enabled by Moon and/or Mars missions. See Volume II, Table 7

Footnote 3. 22% of the critical questions in Life Sciences Discipline Plans are basic science not immediately applicable to Moon and/or Mars missions. See Volume II, Table 3

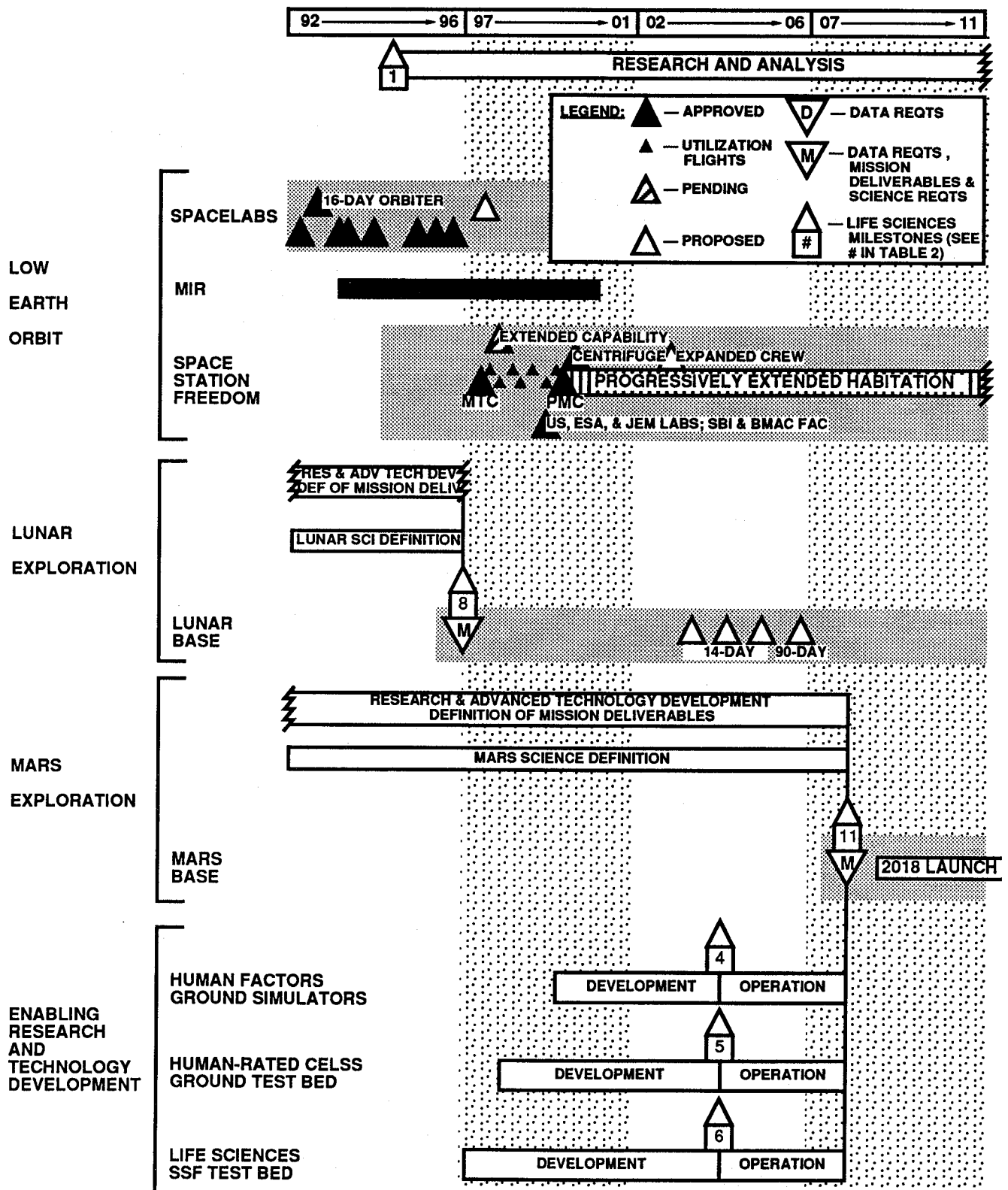
Changing budgets and technical complexities are realities that will affect mission scenarios and milestones, and thus, the execution of this strategy. AMAC assumed that scheduling adjustments, flexible engineering and development planning (e.g., retaining parallel paths of development for contingencies until data is available), and acceleration of appropriate programs could compensate to some degree for any shortfalls and schedule compression. If timely development of the deliverables described in Section II is not possible, the consequence will be increased risk. Frequent updates and refinements of mission scenarios, planned crew activities, and schedule and design decisions as NASA plans for Mars and Moon missions mature, will allow focused life sciences research, thereby decreasing costs and ensuring timeliness.

FIGURE I-2 ENVIRONMENTAL HEALTH AND LIFE SUPPORT SYSTEMS MILESTONES*



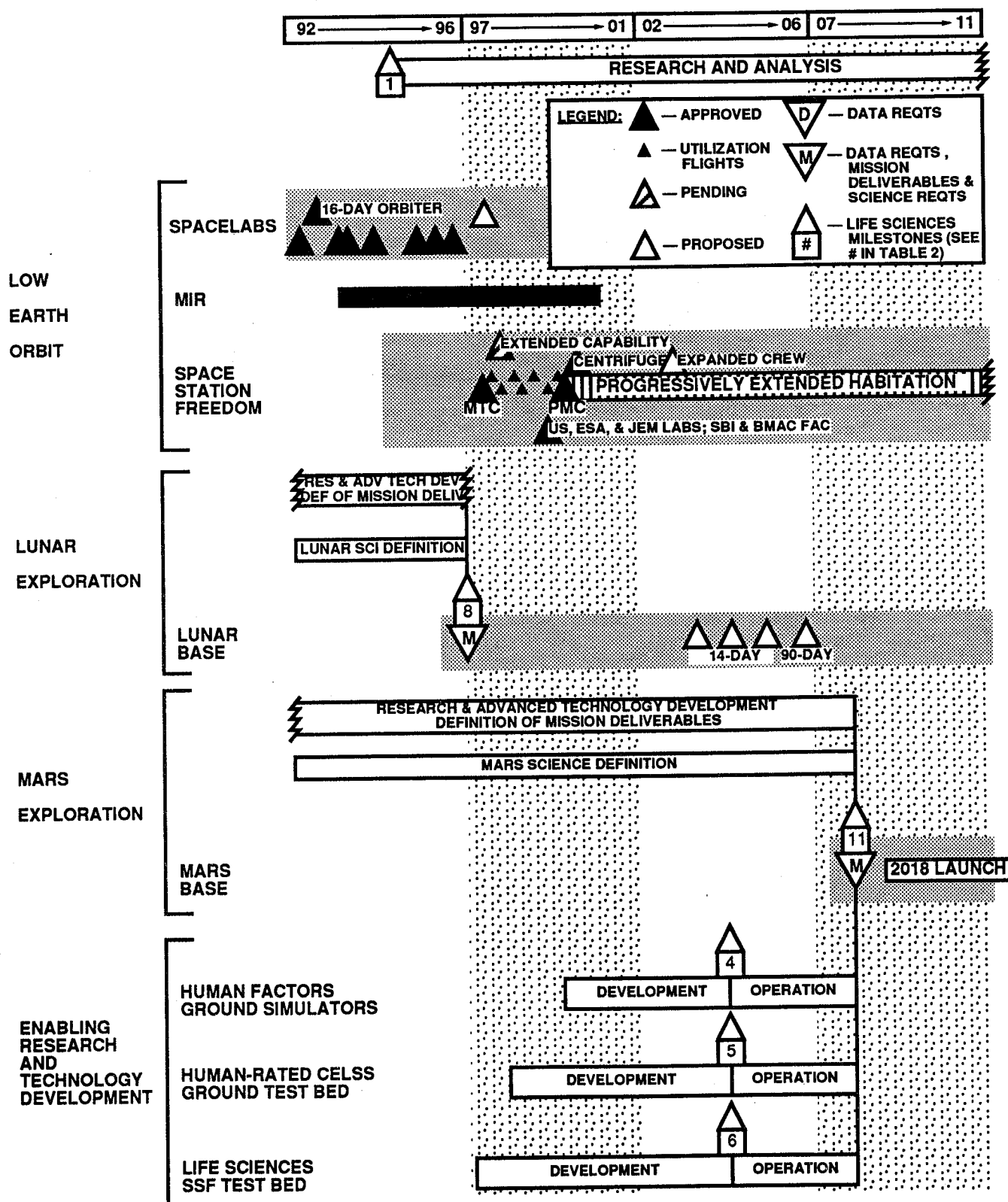
* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

FIGURE I-3 COUNTERMEASURES SYSTEMS MILESTONES*



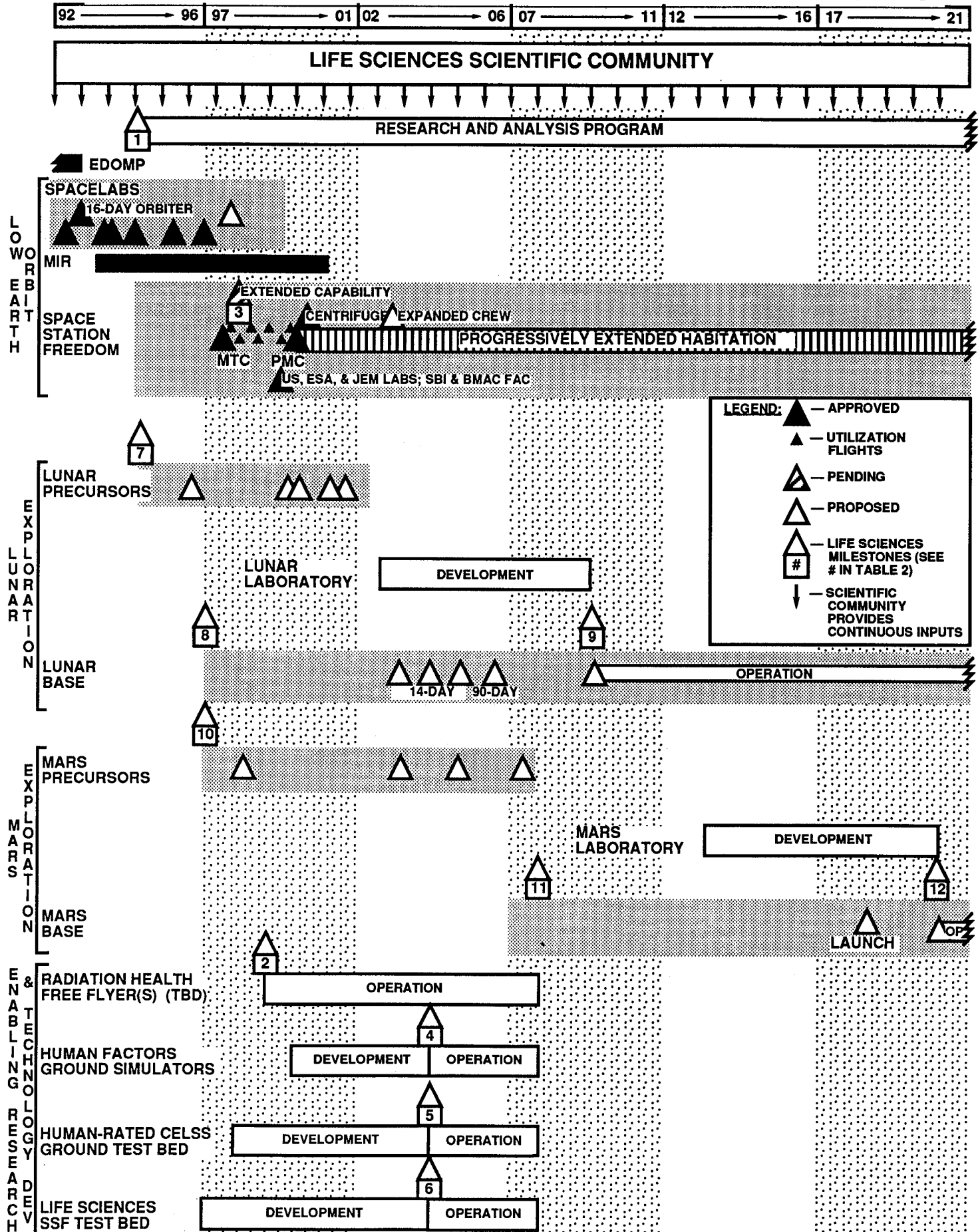
* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

FIGURE I-4 MEDICAL CARE SYSTEMS MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

FIGURE I-5 ACQUISITION OF KNOWLEDGE MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

II. RESOURCE REQUIREMENTS AND MILESTONES FOR DELIVERABLES

A. Introduction

Based on the mission scenarios available and the resources, the milestones and deliverables have been phased in where ground-based research, spacelabs and SSF provide a foundation for future human exploration missions, and the Moon transfer vehicle, orbiter and base (habitat) are considered testbeds for the Mars missions. The phased approach is recommended because:

- It is a prudent way to invest in life sciences research and technology development. Life sciences research characteristically advances through an iterative process of experimentation, data synthesis and hypothesis generation leading to the next phase of experimentation. The phased approach — starting with ground-based research and then refinement of ground models through sequential stages of flight testing and validation — makes sense because knowledge gained from research and operations in early stages can be used to focus and refine the research program in ground-based laboratories, and to define research and operational hardware and procedures for mature mission operational stages.
- It maximizes return on investment. It facilitates focused experiments and missions which fill gaps in scientific and technological knowledge as complexity gradually increases, allowing NASA and national decision makers the ability to develop realistic plans for delivering Mars exploration capability.
- It provides for near-term returns. Answers to most basic science questions which must be obtained to minimize risks during transit and planetary operations will have applications (medicine, biotechnology, agriculture, environmental management, and other human activities that require knowledge of our biological resources) that "improve the quality of life on Earth" and our industrial competitiveness. They are also necessary to fulfill our quest to understand life itself.

Changing budgets and technical complexities are realities that will affect mission scenarios and milestones, and thus, the execution of this strategy. AMAC assumed that scheduling adjustments, flexible engineering and development planning (e.g., retaining parallel paths of development for contingencies until data is available), and acceleration of appropriate programs could compensate to some degree for any budget shortfalls and schedule compression. If timely development of deliverables described in this section is not possible, the consequence will be increased risk. Frequent updates and refinements of mission scenarios, planned crew activities, and schedule and design decisions as NASA plans for Mars and Moon missions mature, will allow more focused life sciences research, thereby decreasing costs and ensuring timeliness. Schedules and deliverables are summarized for the following subcategories:

- Robotic Precursor Missions
- EHLSS — Early Missions Without Bioregenerative Life Support
- Radiation Health
- EHLSS — Later Missions With Bioregenerative Life Support
- Countermeasure Systems For Hypogravity
- Countermeasure Systems For Other Environmental Factors
- Medical Care Systems
- Basic Research and Research Enabled By Moon and Mars Missions
- Utilization of Ground-based Research, Spacelabs, SSF, Moon Base, and Free Flyers.

B. Robotic Precursor Missions

The robotic missions can provide data useful for development of regenerative life support and radiation risk assessment for both Moon and Mars missions. In addition, Mars missions will provide planetary protection information.

Mars mission plans include two Mars Site Reconnaissance Orbiters (MSRO), both launched in one year, and two Mars Surface Rovers (MSVR), launched two years apart to identify and certify locations for landing and establishing a base. The MSRO will map approximately 50 % of the Mars surface over a 20 month period. The two MSVRs involve two year explorations of candidate landing sites to collect data to: (1) verify safe landing and surface base locations; (2) determine the presence of potentially toxic materials; (3) survey the sites for construction plans; and (4) conduct initial scientific investigations (e.g., characterize resource availability).

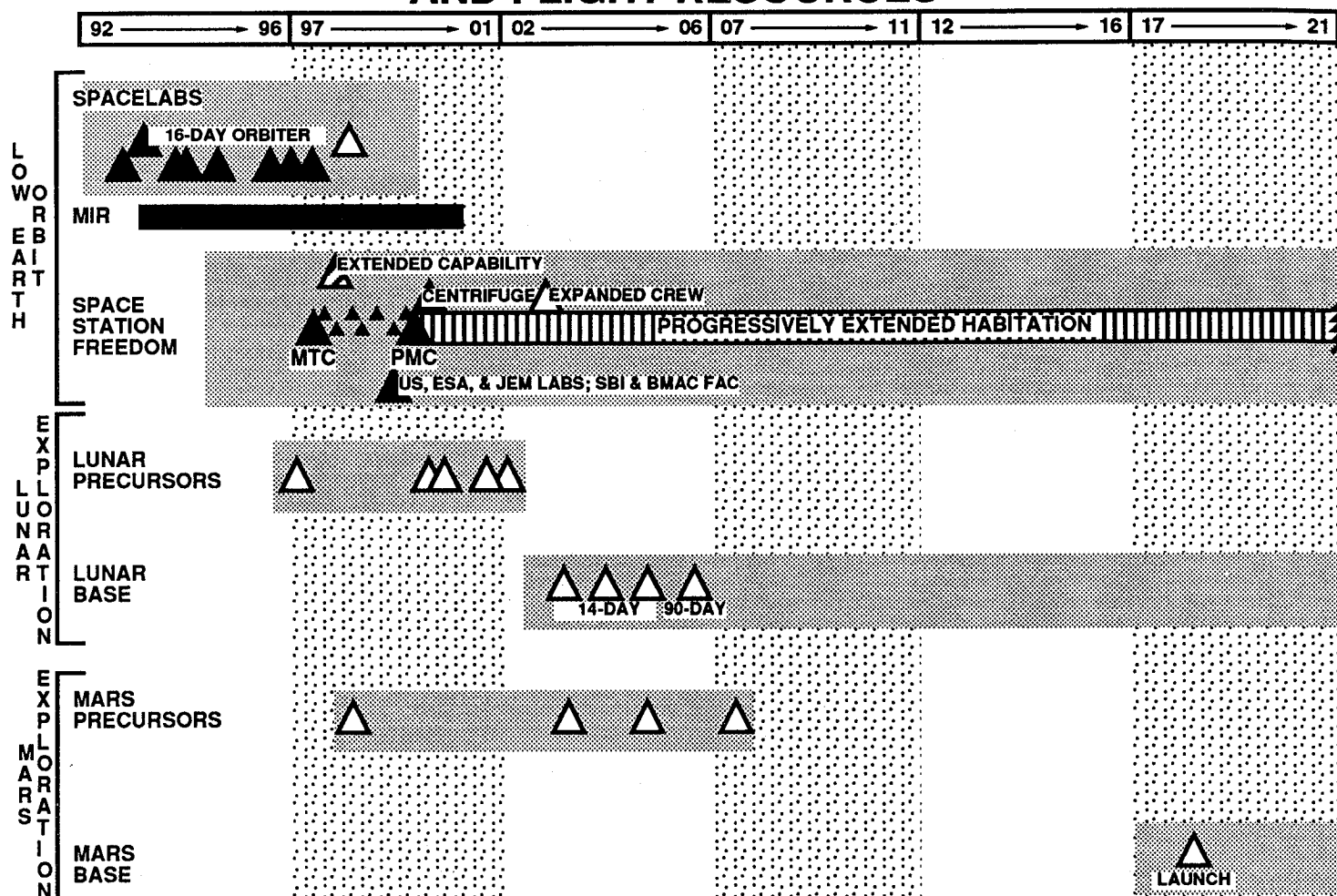
These precursor missions must determine suitability for human habitation and provide *in situ* resource information necessary for development of EHLSS requirements in time to meet delivery schedules for Moon and Mars mission designs. In addition, life sciences must deliver the science requirements necessary for MSRO and MSVR designs. The Planetary Protection Program must enable robotic precursor missions and protect the scientific value of Mars for exobiology studies. Volume II, Table 8 lists the critical questions which would utilize precursor missions. See Tables II-1 and II-2 for deliverables and Figure II-2 for a notional schedule.

C. EHLSS — Early Missions Without Bioregenerative Life Support

Figure II-3 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources and exploration missions.

Deliverables From Life Sciences. Ground-based research and technology and results from Spacelab missions are being used to generate the deliverables for SSF. Experience and research on SSF will form the basis for deliverables for Moon missions which will, in turn, be used for Mars missions (Table II-3).

FIGURE II-1 SPACE EXPLORATION MISSION SCENARIO AND FLIGHT RESOURCES*



*DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

Table II-1
Robotic Precursor Missions — Deliverables From Life Sciences

Data and science requirements for robotic missions:

- Determine the planetary and transit radiation environment, including fluence, flux, energy, and linear energy transfer spectra of the radiation
 - Provide data on radiation shielding characteristics of regolith
 - Provide data necessary to utilize regolith as a raw material for bioregenerative life support
 - Identify potentially toxic materials
 - Provide data on sources of water and oxygen
 - Identify potential sources of back contamination by biological materials
 - Equip orbiters and rovers to study effects of radiation, microgravity, and magnetic fields on suitable organisms
 - Equip orbiters and rovers to incorporate appropriate exobiology studies
 - Develop sterilization technologies for vehicles landing on Mars
 - Develop technologies and protocols for sterilizing, sealing, and monitoring samples returning to Earth
 - Conduct risk analysis for development of policy regarding planetary contamination
- = Required for Mars
•• = Required for Moon and Mars

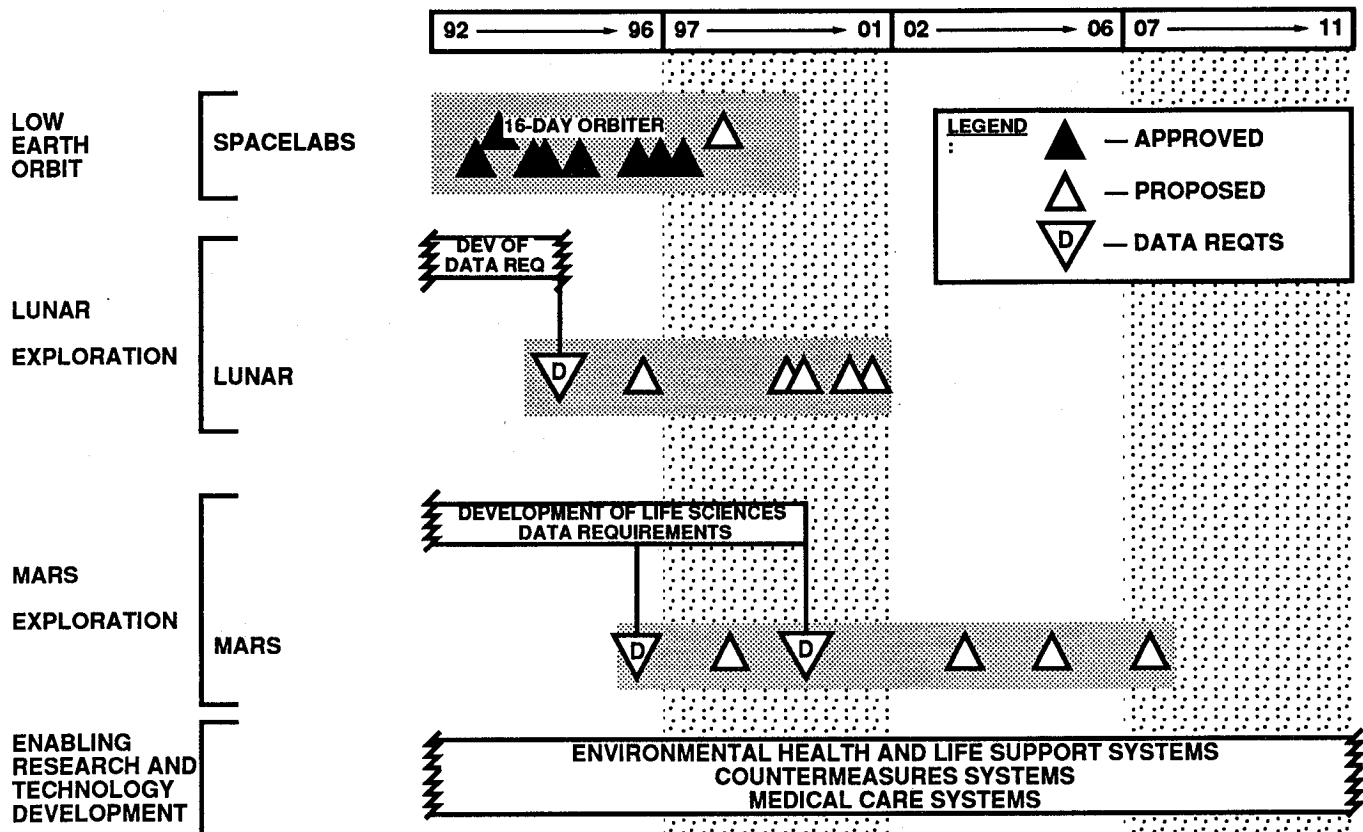
Table II-2
Robotic Precursor Missions — Deliverables To Life Sciences

- Data from robotic missions required for EHLSS, CS, and MCS
 - Data for Planetary Protection Program
 - Experimental results from Exobiology
- = Required for Mars
•• = Required for Moon and Mars

Deliverables To Life Sciences. Until physico-chemical and food storage capabilities are proven, it is prudent for ground-based bioregenerative life support research and development to proceed on a schedule that could support the early manned Mars mission. At that time, effort on bioregenerative systems could be rescoped for later missions and resources could be focused on other high priority early mission requirements. In general, regular updates on planned mission scenarios, crew activities and design decisions will allow focus on optimum use of life sciences resources (Table II-4).

Facility Requirements. Human-rated ground based testbeds will be required to develop and validate the equipment and procedures (including EVA and EHA) under simulated mission conditions to optimize: (1) performance and mental health; (2) crew selection; and (3) environmental health and habitability criteria and monitoring; (4) food, atmosphere, and water suitability; and (5) impact of humans on EHLSS (Table II-5).

FIGURE II-2 LIFE SCIENCES PRECURSOR MISSIONS MILESTONES *



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

Table II-3
Environmental Health and Life Support Systems
Deliverables From Life Sciences

- Define acceptable human health and safety limits for quality and quantity of water, food, and atmosphere
 - Identify requirements and technology for food storage, processing, and preparation
 - Verify life support system capability for EVA and EHA, and provide enhanced technologies
 - Identify requirements and technology for real time monitoring systems for air, water, and surfaces quality
 - Determine requirements for lighting, work-rest schedules, privacy, odor, etc.; and identify means to design habitable facilities
 - Provide basis for optimum design of human-machine interfaces
- = Required for Mars
 •• = Required for Moon and Mars

Table II-4
Environmental Health and Life Support Systems
Deliverables To Life Sciences

- Verify sufficiency of expendable supplies and physico-chemical regenerative technologies for early missions
 - Regular update and refinement of mission scenarios, planned crew activities, and design decisions
- = Required for Mars
 •• = Required for Moon and Mars

Research Initiatives or Major Enhancements. Ground-based programs will have to be focused, expanded, and accelerated. Enhanced, focused flight programs are essential to take advantage of SSF operational experience and research opportunities, and to validate equipment and procedures for extended duration in the microgravity environment. Opportunities on Mir should be aggressively pursued.

Table II-5
Description of Facility Requirements

Human Factors Simulators

Ground-based analogs including transit vehicle simulators and planetary habitats simulators will be used as testbeds for medical protocols and countermeasures development.

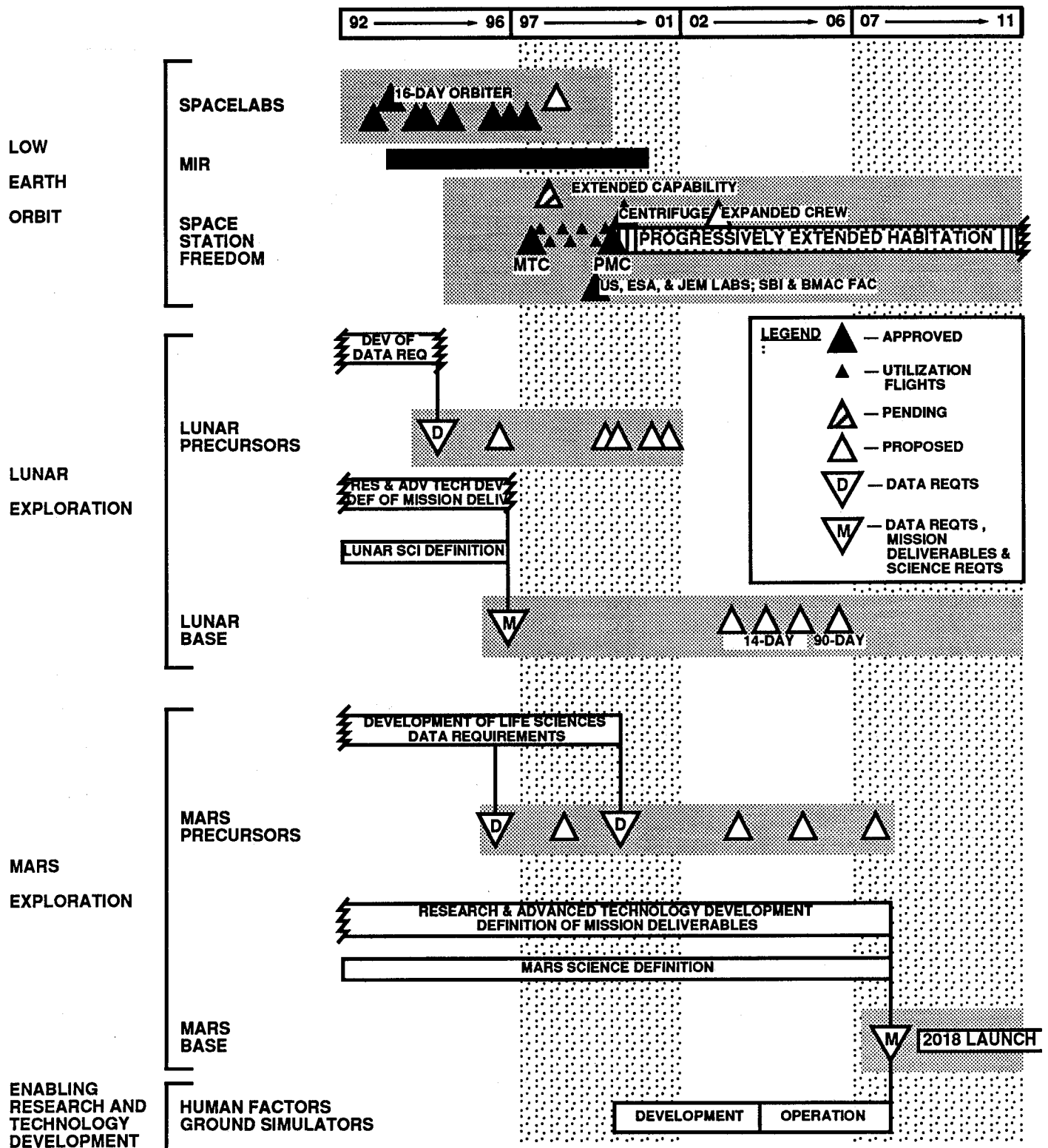
Human-Rated Ground-Based CELSS Testbed

Will be used to develop and validate research and technologies required for an operational bioregenerative life support system and to address environmental, health, and safety issues.

Life Sciences SSF Testbed

Will be used for validation of life support, medical care and countermeasures under operational conditions for transit vehicles.

FIGURE II-3 ENVIRONMENTAL HEALTH AND LIFE SUPPORT — EARLY MISSIONS MILESTONES *



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

D. Radiation Health

Figure II-4 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources and exploration missions.

Deliverables From Life Sciences. Life sciences must provide the human dose limits for space missions (proton and GCR) and the science and technology base necessary to design transit vehicles and planetary bases with shielding and safe havens that satisfy those limits (Table II-6).

Table II-6
Radiation Health — Deliverables From Life Sciences

- Characterize deep space radiation environments
- Determine the human radiation dose limits for space missions (protons and GCR)
- Provide solar event warning capability
- Provide protection from radiation (protons and GCR)
 - = Required for Mars
 - = Required for Moon and Mars

Deliverables To Life Sciences. Life sciences research and advanced technology programs require data which characterize the deep space radiation environment; and the radiation shielding characteristic of spacecraft materials and regolith (Table II-7).

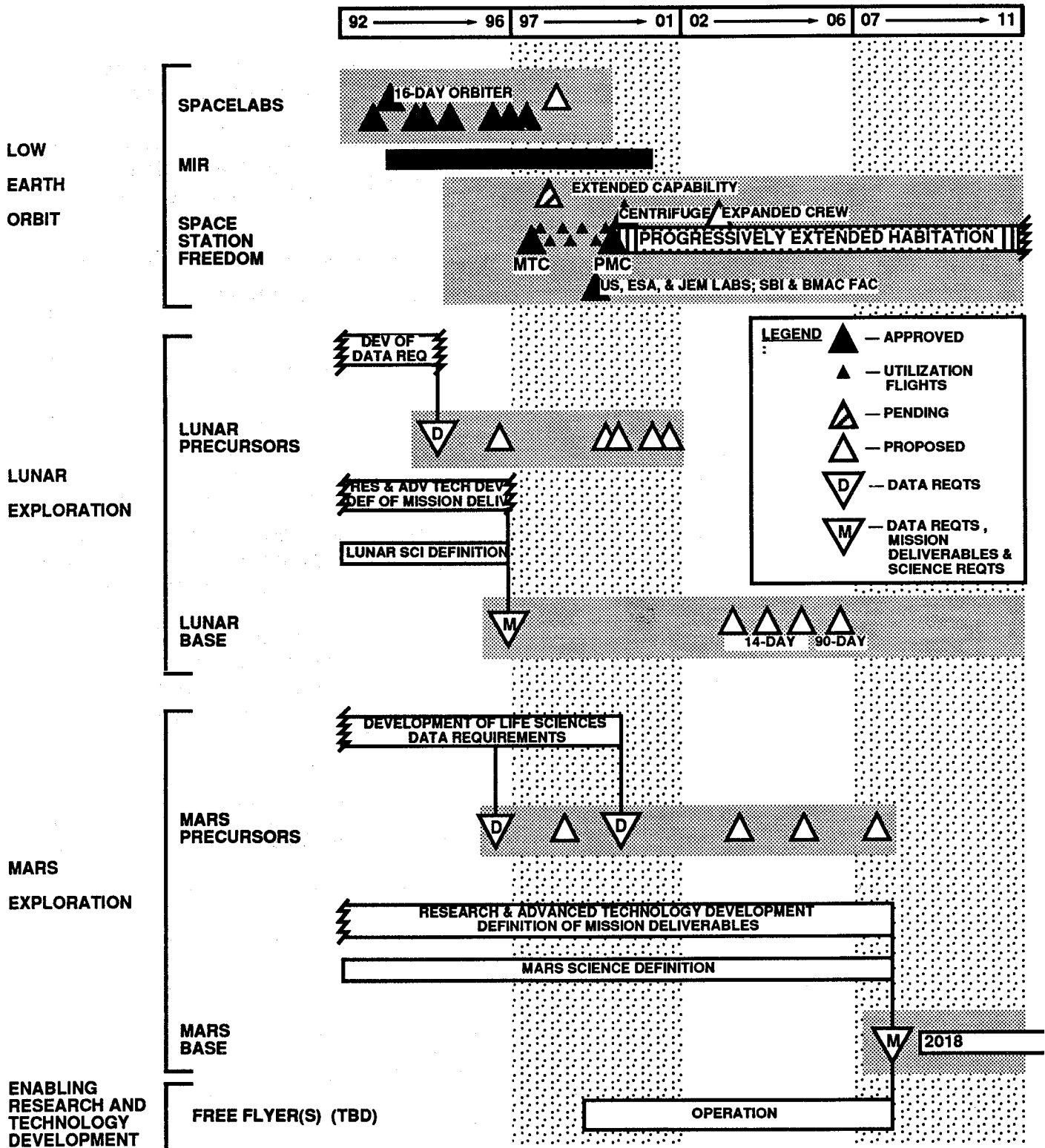
Facility Requirements. Availability of sufficient beam time at an HZE ground source facility is absolutely essential. A free flyer capable of supporting appropriate biological specimens outside the Earth's magnetosphere would allow early characterization of the radiation environment and its biological effects. Early experimental data would allow focused research, reduce risk, and resolve the uncertainties regarding HZE particles (Table II-6).

Table II-7
Radiation Health — Deliverables To Life Sciences

- Data on deep space radiation environment from precursor missions and any other deep space missions
- Data on the radiation shielding characteristics of spacecraft materials and regolith
 - = Required for Mars
 - = Required for Moon and Mars

Initiatives or Major Enhancements. Ground-based and flight research and technology programs must be accelerated and expanded to provide timely inputs to planning and design of Moon and Mars missions.

FIGURE II-4 RADIATION HEALTH MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

E. Life Support — Later Missions With Bioregenerative Life Support

Figure II-5 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources with focus on the Mars exploration missions.

Deliverables From Life Sciences. Life sciences will provide the design criteria, models, and trade-off studies for crew sustenance for different spacecraft and habitat designs (Table II-8).

Table II-8
Life Support — Deliverables From Life Sciences

- Provide criteria for design and operation of bioregenerative components of a life support system that, as a minimum, provides partial recycling of oxygen, water, carbon dioxide, and waste
 - Provide trade-off analysis comparing expendable, PC, integrated PC-bioregenerative, and predominantly bioregenerative life support systems
 - Provide criteria for design and operation of a predominantly bioregenerative life support system
 - Identify storage, processing, and preparation technologies for food produced in bioregenerative life support systems
 - Provide mathematical models for simulation, design, and operation
 - Provide technologies to use regolith as a resource in bioregenerative life support systems
 - Establish nutritional and behavioral requirements for fresh food on long duration missions
- = Required for Mars
•• = Required for Moon and Mars

Deliverables To Life Sciences. Data on regolith and radiation environments necessary for design of regenerative life support systems (Table II-9).

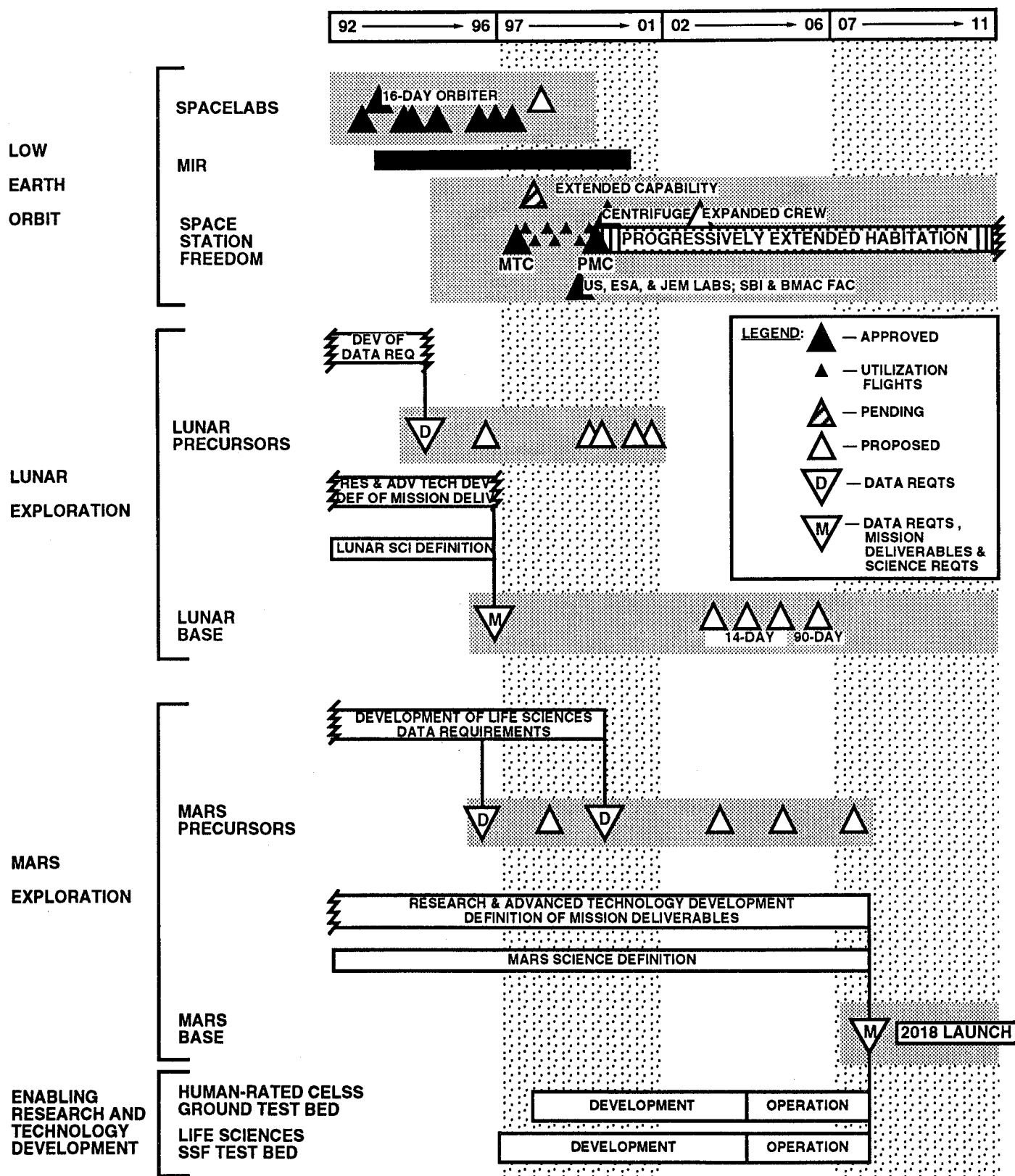
Table II-9
Life Support — Deliverables To Life Sciences

- Data on oxygen and water availability
 - Data on composition and characteristics of regolith
 - Data on radiation environment throughout mission scenario
- = Required for Mars
•• = Required for Moon and Mars

Facilities Requirements. Applicable research will be conducted in the ground-based human-rated controlled Environmental Life Support System Testbed. SSF Life Sciences Testbed (including an evolutionary prototype operational CELSS) (Table II-5).

Initiatives or Major Enhancements. The ground-based CELSS (e.g., CELSS Breadboard Test Facility, CELSS RTOP) and plant biology research programs will require significant enhancements. Ongoing (Spacelab) and planned research (SSF

FIGURE II-5 BIOGENERATIVE LIFE SUPPORT — LATER MISSIONS MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

CELSS Test Facility and plant research in the Gravitational Biology Facility) should be accelerated and enhanced.

F. Countermeasures for Hypogravity Effects

Figure II-6 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources and exploration missions.

Deliverables From Life Sciences. It is very likely that human adaptation and thus countermeasure requirements will be different for SSF, Moon, and Mars missions (Table II-10).

Table II-10
Countermeasures for Hypogravity Effects
Deliverables From Life Sciences

- Provide the criteria for design and operation of CS (e.g., exercise, dietary, pharmacological, mechanical, physiological, training) for human adaptations (e.g., musculoskeletal, cardiovascular, physiological, neurological, and cellular) to microgravity
 - Provide the criteria for design and operation of CS for human adaptations to the Moon (0.16g) environment
 - Provide the criteria for design and operation of CS for human adaptations to the Mars (0.38g) environment
 - Provide criteria for design and operations of CS for readaptation to Earth
- = Required for Mars
 - = Required for Moon and Mars

Deliverables To Life Sciences. The expected timelines are necessary because human adaptation and appropriate countermeasures will vary with sequence, gravity level, duration of exposure, and human activity. Limited resources must be focused on a restricted set of highly probable scenarios (Table II-11).

Table II-11
Countermeasures for Hypogravity Effects
Deliverables To Life Sciences

- Mission scenarios, including a timeline with duration of exposure to the various levels of hypogravity and a description of the expected activity (including EVA and EHA) during increments
- = Required for Mars
 - = Required for Moon and Mars

Facilities Requirements. Countermeasure systems will utilize the SSF Life Sciences Testbed. However, equipment specifically for developing, testing, and verifying countermeasures will be required. Neurolab, a Spacelab mission already included in the Life Sciences Division Strategic Plan, will provide scientific knowledge and information necessary for design of countermeasures applicable to SSF, Moon, and Mars missions. Advanced instruments (e.g., nuclear magnetic resonance (NMR) imaging, virtual reality) specifically designed for compatibility with SSF, will facilitate

both basic research and the development of countermeasures. Larger SSF crew size (e.g., eight) and longer rotation periods (e.g., >180 days) are needed when the SSF Life Sciences Testbed is operational. If microgravity countermeasures are ineffective for longer durations, a low Earth orbit artificial g testbed will be required (Table II-5).

Initiatives or Major Enhancements. Ground-based and flight programs will have to be enhanced to conduct fundamental microgravity research and to take advantage of operational experience on SSF. An initiative to determine the consequences of long-duration exposure to 0.16g and 0.38g (especially after a period in microgravity) is essential for planning and execution of Moon and Mars missions. An initiative to evaluate the usefulness of human centrifuges on planetary and transit vehicles might provide enormous benefits to human safety and performance, and could potentially decrease the complexity of countermeasure systems.

G. Countermeasures to Other Environmental Factors

Figure II-7 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources and exploration missions.

Deliverables From Life Sciences. Russian and U.S. space flight experiences suggest that improved countermeasures are more critical for longer duration missions. Life sciences must deliver increasingly sophisticated and complex systems as the missions proceed from long-duration SSF to the Moon base and to Mars bases (Table II-12).

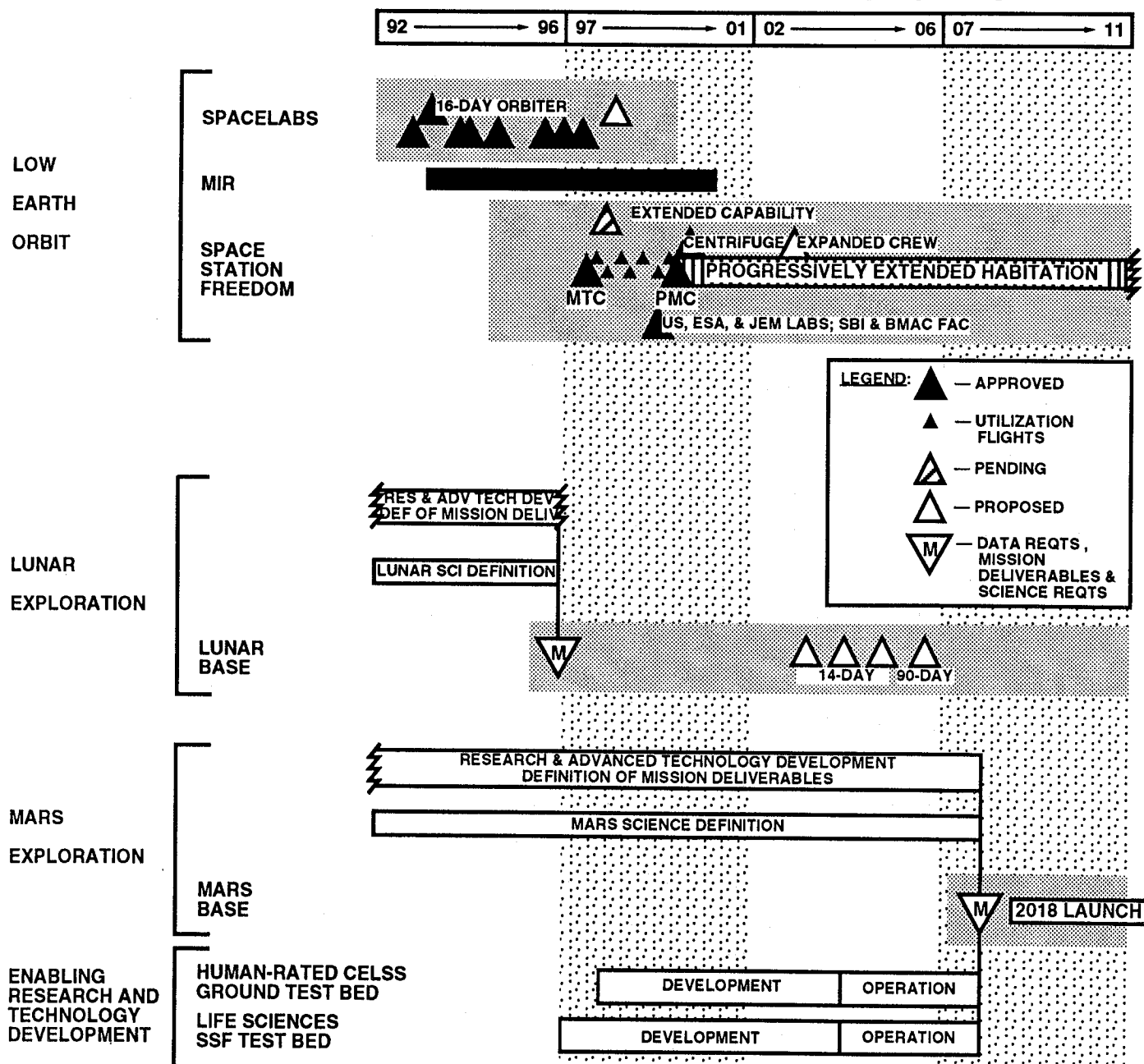
Table II-12
Countermeasures to Other Environmental Factors
Deliverables From Life Sciences

- Provide the criteria for design and operation of countermeasures for human responses to space vehicle and planetary base environments not specifically related to hypogravity (e.g. atmosphere, toxins, food quality, confined volume, light, restricted human interaction, privacy, recreational activities, esthetic diversity, and stress)
 - Provide criteria and protocols for crew selection, training, and scheduling to mitigate affects of space flight environmental factors
 - Provide trade-off studies for countermeasure alternatives
- = Required for Mars
 - = Required for Moon and Mars

Deliverables To Life Sciences. Except for a central core, scheduling and focus of life sciences research is dependent upon mission scenarios and crew activities including EVA and EHA (Table II-13).

Facilities Requirements. Applicable research will be conducted in the Human Factors Simulators, Human-Rated CELSS Testbed, and SSF Life Sciences Testbed discussed in Section II - C, E and F. However, task-specific instrumentation and hardware will be required (Table II-5).

FIGURE II-6 HYPOGRAVITY COUNTERMEASURES SYSTEMS MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

Table II-13
Countermeasures to Other Environmental Factors
Deliverables To Life Sciences

- Mission scenarios including timelines for activities including EVA and EHA
 - = Required for Mars
 - = Required for Moon and Mars

Initiatives or Major Enhancements. Ground-based programs will have to be enhanced. Countermeasure capabilities will evolve as the duration of Spacelab and SSF missions increases. Enhancements will be required for long-duration Moon orbiter, Moon base, and Mars missions.

H. Medical Care Systems

Figure II-8 provides a notional schedule for life sciences deliverables and facility requirements in relationship to current flight resources and exploration missions.

Deliverables From Life Sciences. Development of Medical Care System deliverables will be phased, evolving from increasingly longer duration experience on SSF (Table II-14).

Table II-14
Medical Care Systems — Deliverables From Life Sciences

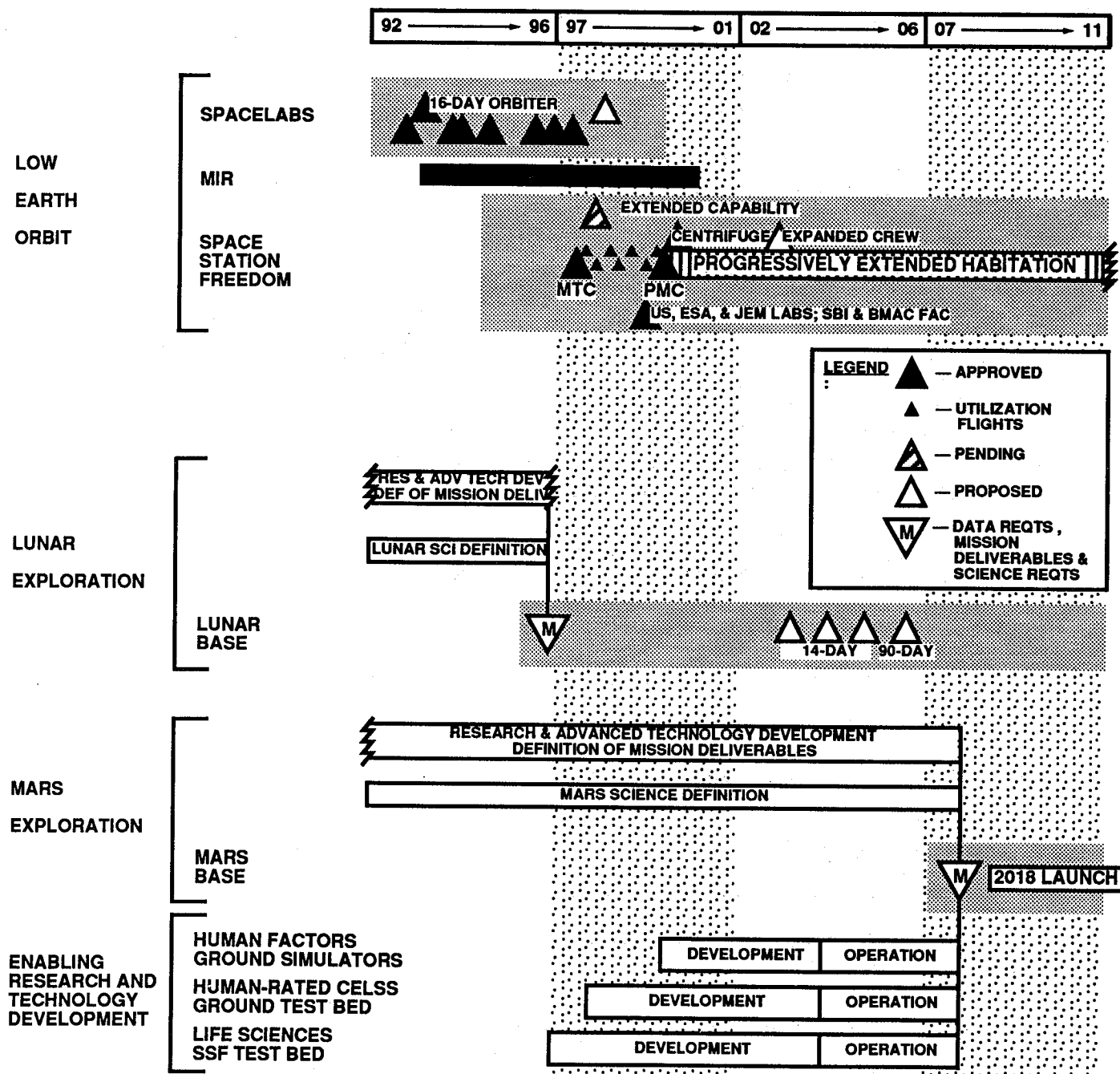
- Provide the criteria necessary to design and equip health maintenance facilities (including EVA and EHA risks) for Moon and Mars transit vehicles and bases
- Develop preventive medicine, and monitoring, therapy and treatment protocols for exploration missions
- Provide telemedicine capability for medical contingencies
- Provide medical criteria for crew selection
- Develop the medical training protocols for exploration mission crews
- Provide protocols for post mission health monitoring and care
 - = Required for Mars
 - = Required for Moon and Mars

Deliverables to Life Sciences. Medical care requirements are dependent on mission scenarios. For example, they may be minimized for Earth orbit and Moon operations, where rescue times are short (Table II-15).

Table II-15
Medical Care Systems — Deliverables To Life Sciences

- Mission scenarios including timelines and activities such as EVA and EHA.
 - = Required for Mars
 - = Required for Moon and Mars

FIGURE II-7 OTHER COUNTERMEASURES SYSTEMS MILESTONES*



*DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

Facilities Requirements. Medical Care Systems development will be conducted in the Human Factors Simulators, Human Rated CELSS Testbed, and SSF Life Sciences Testbed discussed in Section II-C, E and F. Medical Care System specific instrumentation and hardware will be required (Table II-5).

Initiatives or Major Enhancements. Extended durations and extremely long distances will require an unprecedented level of inflight medical care capability. Current resource levels cannot support development of those systems.

I. Acquisition of Knowledge

Planning for scientific investigations is an integral part of operations and systems development planning for Moon and Mars missions. The university, commercial, and private scientific community will participate in establishing specific Science Plans and development of Science and Technical Requirements Documents that will be used to design Moon base, Mars transit, and Mars base laboratories (Table II-16). Figure II-9 provides a notional schedule for life sciences deliverables and illustrates its continuous significant involvement of the life sciences scientific community.

Table II-16 Acquisition of Knowledge — Deliverables From Life Sciences	
••	Provide science and technology requirements necessary to design the laboratory for Moon base
•	Provide science and technology requirements necessary to design Mars transit vehicle research facilities
•	Provide science and technology requirements necessary to design laboratory for Mars base
••	Provide research proposals for SSF, Moon, Mars transit vehicle, and Mars base laboratories
•	= Required for Mars
••	= Required for Moon and Mars

J. Utilization of Ground-Based Research, Spacelab, SSF, Moon Base, and Free Flyers

Research and technology development for exploration missions will involve a wide diversity of ground-based research and flight platforms. Requirements for the constrained programs for EHLSS, CS, and MCS are summarized in Appendix H; and for robust programs, in Volume II, Table 2. The notional schedule in Figure II-9 identifies the flight resources available to support specific phases of the exploration program. Existing Life Sciences Programs are appropriately balanced between human exploration and basic science.

1. Ground-Based Research

Ground-based research provides the science and technology foundation for flight research. In fact, it is used extensively to develop alternatives and screen options in order to reduce the risk and need for costly space flight experiments. Accordingly,

95% of the critical questions require additional ground-based research (Volume II, Table 3).

2. Spacelabs

A continued Spacelab mission series with extended duration is required to obtain information for environmental life support and monitoring of critical health parameters, countermeasure development and testing, and verification of medical care procedures. If Spacelab resources were available, they could contribute to addressing 66% of the critical questions (Volume II, Table 4). They would be particularly useful for technology validation and testing for EHLSS, and for characterizing the "normal" physiological and behavioral responses to space flight essential for CS and MCS. They will continue to provide the experimental foundation necessary to elucidate the mechanisms whereby gravity or its absence affect living systems.

3. Space Station Freedom Utilization

Permanent presence in space on SSF is the first step in the Mission from Planet Earth (MFPE). SSF will provide the U.S. and its international partners the ability to develop, test, and validate prototype Moon and Mars EHLSS, CS and MCS. Beginning during MTC:

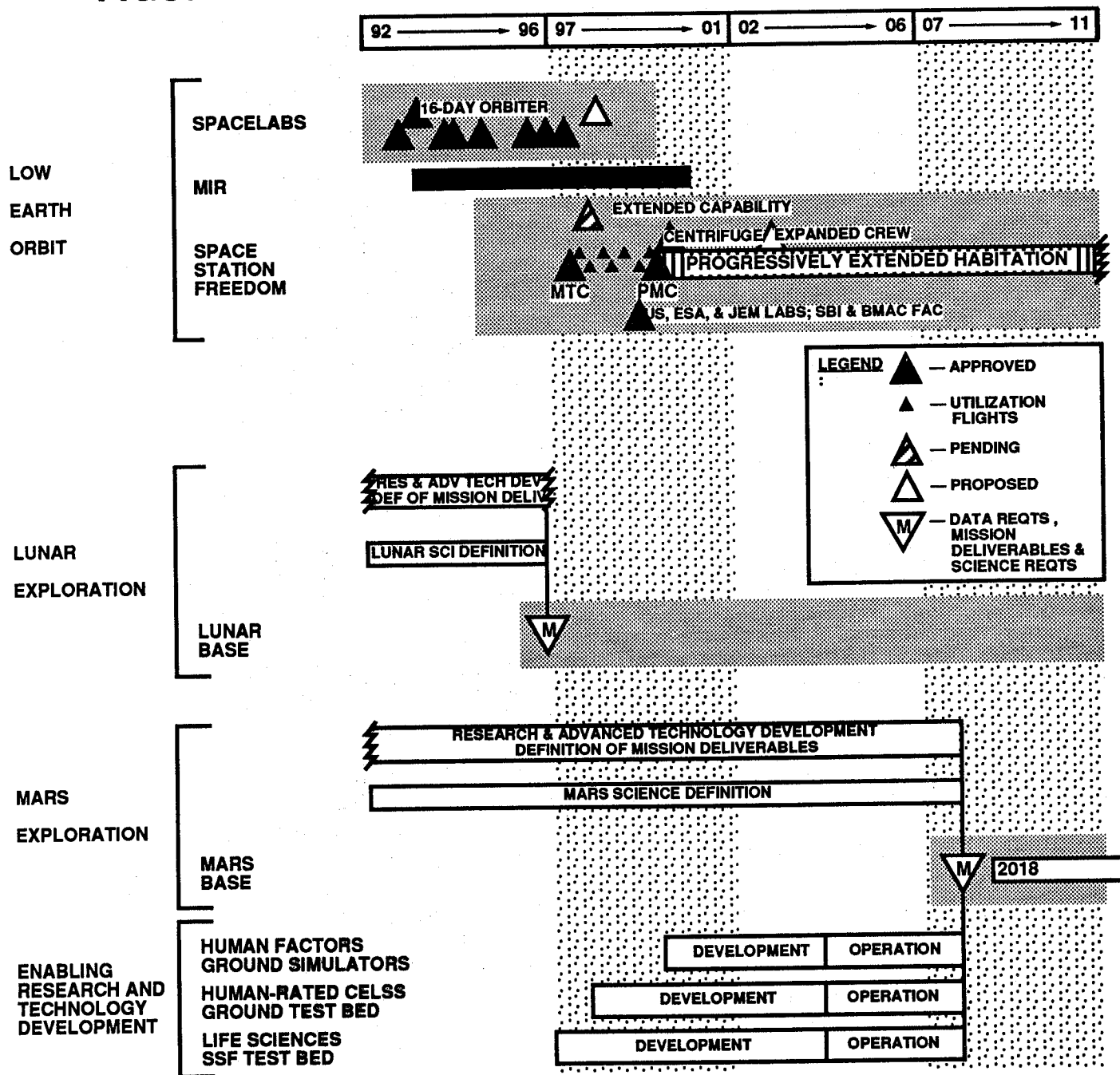
- (1) The BMAC Program will focus on developing and validating countermeasures for progressively longer duration on-orbit crew times
- (2) Research programs will focus on the physiological and behavioral adaptations to flight in order to: (a) define the normal envelope for parameters in the space flight environment; (b) understand the underlying mechanisms; and (c) develop models and simulations
- (3) Repeated EVA during the construction phase will allow accumulation of data and experience which will facilitate advanced equipment and procedures for exploration
- (4) Gravitational biology studies will focus on microgravity and radiation interactions and the impact of microgravity on plant structure and function.

Extended Man-Tended Capability (EMTC) may provide information on long duration exposure. This gradual buildup of duration will provide early data for exploration and will improve the productivity of SSF during early Permanently Manned Capability (PMC).

During PMC, the Crew Health Care System (CHeCS) will provide operational medical care experience. Subsystems include a Health Maintenance Facility (HMF), Environmental Health System (EHS), and a supporting hyperbaric chamber.

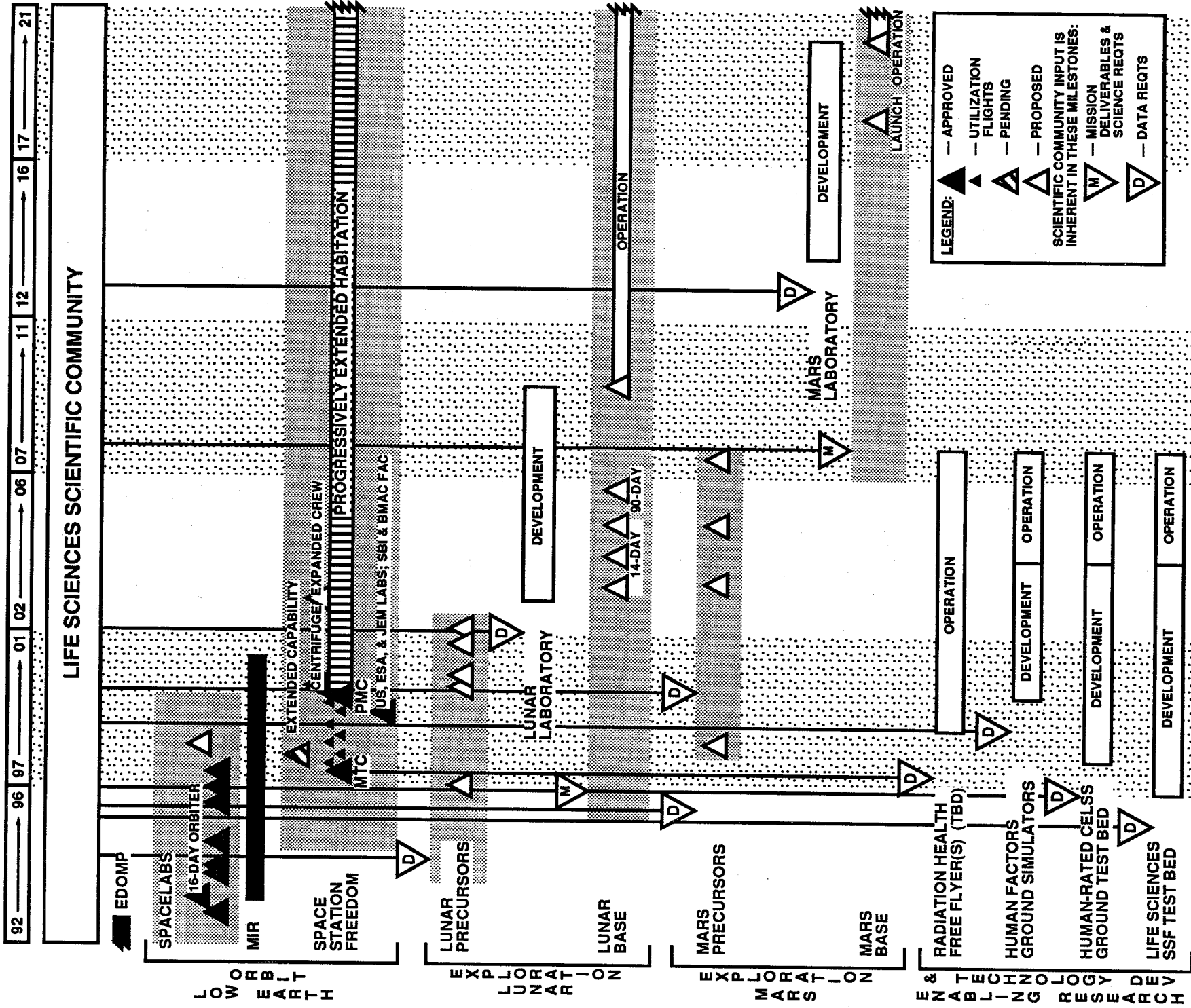
During PMC, SSF provides unique space flight advantages — extended duration, technically advanced facilities, inflight sample preservation and analysis, sufficient sample size (replications), variable g — to address biological questions. While some questions can be investigated on short-duration space flights provided by Spacelabs,

FIGURE II-8 MEDICAL CARE SYSTEMS MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

FIGURE II-9 ACQUISITION OF KNOWLEDGE MILESTONES*



* DATES ARE NOTIONAL AND DEPEND UPON AVAILABLE RESOURCES AND TECHNOLOGY DEVELOPMENT

recoverable satellites, and even sounding rockets, many questions require a long-duration facility such as SSF. For example, many biological processes (e.g., organism development, multigeneration cycles, and adaptation) simply require extended periods of time to occur. Also, the answers to many biological questions can only be provided through extended duration experiments where the results of on-orbit observation and analysis can be used to modify experimental parameters of ongoing or sequential follow-on experiments. Technically advanced facilities and on-orbit analysis will, for the first time, allow investigations involving key unstable biological components that require immediate analysis, and structures, products, and phenomena that are modified during reentry and return. Advanced sample preparation and preservation technology will greatly enhance the science return from on-orbit experiments by increasing the preservation options and variety of samples available for more sophisticated ground-based analysis.

Inherent biological variability requires that sufficient time and sample number be provided for an effect to be unambiguously manifested. Our ability to clearly interpret past U.S. and international life sciences flight experiments and provide operational remedies has often been limited because there are too few replications. SSF capabilities promise to provide the time and number of samples for clear interpretation of statistically valid results. Furthermore, a continuously operating laboratory in space will allow replication of experiments and eliminate the current two-plus year delay required to manifest follow-up experiments to take advantage of exciting discoveries.

SSF will allow scientists to take advantage of biological diversity by selecting from the full spectrum of biological species to address questions. Most importantly, it will allow them to match the question to the most appropriate biological model. The ability to use well characterized specimens that have been used extensively for research on Earth will: (1) enhance the interpretability of results and development of a consensus in the scientific community because extensive knowledge bases already exist; (2) decrease the need for NASA-sponsored preparatory ground-based experiments; and (3) shorten the time course and reduce the cost of acquiring answers to critical life sciences questions. Furthermore, access to species not previously available in space flight will attract an expanded scientific community and enrich the program. The Space Physiology Facility, Gravitational Biology Facility, Centrifuge Facility, CELSS Test Facility, and BMAC equipment on SSF will greatly enhance our ability to conduct the kinds of interspecies comparative studies that have always been a fundamental tool of life sciences research.

Small centrifuges for lower organisms, cell cultures, and small plants and animals in conjunction with the Centrifuge Facility for larger plants and animals will provide the ability to manipulate gravitational levels from near zero to 2g for a broad diversity of species. This capability will allow control of gravity as a variable in a manner analogous to the way light intensity, temperature, nutrient levels, drug dosages, etc., have always been manipulated to elucidate the fundamental mechanisms and processes involved in the structure and function of living systems. Furthermore, they will allow us to explicitly evaluate the effect of Moon (0.16 g) and Mars (0.38 g) gravity levels on candidate organisms for bioregenerative life support systems for Moon and Mars bases. In addition, experiments with animals as surrogates for humans will allow

predictions of the effects of Moon, Mars, and transit vehicle gravity regimes on humans.

When the Life Sciences SSF Testbed becomes operational it will be used for validation of life support, medical care, and countermeasures under operational conditions for transit vehicles.

Finally, SSF provides the real lessons learned from the experiences of building, operating, living, working, and conducting research in a large, increasingly complex, long-duration facility in space. The Advisory Committee on the Future of the U.S. Space Program, 1990, and the Report of the Synthesis Group on America's Space Exploration Initiative, 1991, recommendations on the importance of SSF are substantiated by the fact that over 83% of the critical questions in life sciences need SSF (Volume II, Table 5). The Centrifuge Facility will support over 36% of the critical questions (Volume II, Table 6).

4. Moon Base Utilization

Moon base facilities will provide the opportunity to expand research that will reduce the logistics burden for Moon operations and enhance human performance on Moon and Mars surfaces. A research site outside the Earth's magnetosphere will facilitate detailed study of GCR, and the base will be an operational test of radiation shielding. Moon operations will accelerate the development, testing, and validation of CS and MCS, and will provide extensive information on 0.16 g operations. Extensive experience with life support systems will accelerate and refine EHLSS. A Moon base testbed for bioregenerative components of an integrated PC-bioregenerative system will accelerate CELSS development. Moon bases allow evolutionary development, testing, and verification of EHLSS, CS and MCS systems for the Mars missions. Research equipment for Moon missions will allow study of the effects of radiation and hypogravity (microgravity and 0.16g) on suitable organisms; and the conduct of early exobiology experiments. Even after consideration of the advantages of conducting research in low Earth orbit, 65% of the critical questions would benefit from access to Moon bases (Volume II, Table 7).

Exploration planning includes an Initial Operating Capability (IOC) on the Moon that provides a single, integrated habitat that supports a crew of five for 14 days. External shielding will provide radiation protection, and the habitat will include life support, crew accommodations, health care equipment, science facilities, and utilities.

The life support system is expected to be an advanced SSF regenerative system, with greater than 98% oxygen recovery, hygiene water processor, and nonexpendable water polisher/bacteria barrier. The Next Operating Capability (NOC) will extend the surface infrastructure to support crews for up to 90 days and could include prototype Mars technology. The NOC2 habitat at a second site will utilize life support technology planned for the Mars mission. This advanced system will incorporate waste processing to reduce requirements for consumables. It will also include advanced countermeasure and medical care systems.

5. Free Flyers

The utilization of reusable, low cost, free-flying platforms should be considered to address the research thrusts that cannot be accommodated with the previously described facilities. Planning for free flyers should be tailored to the priorities and schedules necessary to accelerate or increase the efficiency of efforts to develop solutions for Moon and Mars missions. They would enable investigations of microgravity and radiation effects on living organisms, including plants, rodents, cell and tissue cultures, and other biological specimens. A recoverable should have the capability for access to unique orbits (e.g., polar) for extended periods (e.g., 30 to 60 days). A recoverable would enable real-time active measurements of all components of GCR and investigation of the interaction between microgravity and radiation. These studies would validate ground-based predictions and models in the space environment. Thirty percent of the critical questions would benefit from access to free flyers (Volume II, Table 9).

III. PROVIDING ACCESS TO SPACE FOR LIFE SCIENCES BASIC RESEARCH

A. Basic Science Not Immediately Applicable to Moon and Mars Missions

Throughout its evolution, life on Earth has been exposed to the constant force of gravity. Therefore, it is axiomatic that gravity helped shape and continues to influence the structure, function, and ongoing evolution of all living organisms. Because of its pervasive influence, understanding the effects of gravity on life is a fundamental question of substantial, inherent scientific value in our quest to understand life. Knowledge of the effects of gravity on lower organisms, plants, humans, and other animals, as well as elucidation of the basic mechanisms by which these effects occur, will be of direct benefit to: (1) the quality of life on Earth through applications in medicine, agriculture, industrial biotechnology, environmental management, and other human activities dependent on understanding biological resources; (2) understanding the impact of, and providing countermeasures for, long-term exposure of humans to the microgravity of space flight and the partial gravity of Moon and planetary bases; and (3) development of bioregenerative life support systems for use on human exploration missions.

Space flight provides the only environment in which the force of gravity can be removed or discrete levels of gravitational force between 0 and 1 g can be provided to address critical scientific questions. Variable g hardware will allow control of gravity as a variable analogous to the way in which light intensity and quality, temperature, nutrient levels, drug dosages, etc., have always been manipulated to elucidate the fundamental mechanisms and processes involved in the structure and function of living systems. Also, space is the only environment in which other fundamental biological processes and mechanisms can be studied in the absence of coupled and sometimes overwhelming effects of gravity.

The closed environment of spacecrafts provides a unique opportunity to conduct controlled experiments to investigate the impacts of environmental factors such as atmosphere, light, confined space, radiation, and their interaction with gravitational force. Twenty-two percent (22%) of the critical questions in the Life Sciences Discipline Science Plans (Volume II, Table 2) address research which is not applicable to MFPE missions. The existing Life Sciences Program provides appropriately balanced support for this research consistent with NASA goals.

Moon and Mars missions will provide both the opportunity to conduct research, foster science and math education, and spark the imagination of scientists and the American public, adding impetus for space sciences research in general. The Life Sciences Program must maintain its balanced approach.

B. Inherent Scientific Merit of the Science and Technology Research that Supports Moon and Mars Missions

Most of the science required for Moon and/or Mars missions has inherent scientific value and is justifiable on its own merit. In many instances the experimental data necessary to understand the structure and function of living systems is the same fundamental data required for applications that would improve "quality of life on Earth," or which would allow design of spacecraft, space bases, and space suits that will enable human exploration of our solar system. Both "science for the sake of science," (including understanding of the origin, evolution and distribution of life in the universe) and "human health and well-being in space" and will undoubtedly benefit from the understanding of physico-chemical processes, and biological perception and transduction of gravity.

C. Science Enabled by Moon and Mars Missions

Moon and Mars missions will provide broad impetus for science and accelerate acquisition of knowledge in gravitational biology across all disciplines. The following discussion focuses only on those areas of science which will be specifically facilitated or enhanced by Moon and Mars missions, immediately applicable to enabling those missions.

1. Introduction

The Exobiology Program, the scientific study of Mars, and the enabled science that can be accomplished on such a mission are among the primary justifications for going to Mars. The Synthesis Group Report and NASA Office of Exploration planning (Appendix G) emphasize that "planning for scientific investigations shall be an integral part of operations and exploration missions." Mars and Moon missions enable activities that offer promising and unique science opportunities. Of twelve Life Sciences Division disciplines, seven have critical questions¹ enabled by these missions.

Table III-1
Life Sciences Disciplines Enabled by Mars and Moon Missions

Exobiology
Cell and Developmental Biology
Neuroscience
Regulatory Physiology
Cardiopulmonary
Musculoskeletal
Behavior, Performance and Human Factors

Footnote 1. 12% of the critical questions identified in Life Sciences Division Discipline Science Plans are enabled by Mars and or Moon missions. See Volume II Table 2.

2. Exobiology

The Exobiology Program seeks to understand the origin, evolution, and distribution of life and life-related molecules in the universe. It is a highly interdisciplinary program encompassing such diverse research areas as chemical evolution (the history of carbon and carbon-containing molecules in the universe), microbiology, paleomicrobiology, organic geochemistry, geology, planetology, radio astronomy, and the Search for Extraterrestrial Intelligence (SETI), to name a few. The program requires extensive ground-based research in all of the areas mentioned, as well as the opportunity for long-term orbital research (e.g., on SSF) and studies of interstellar molecules and extraterrestrial bodies, such as comets, asteroids, meteorites, and planets. All evidence suggests that the origin and evolution of life is inextricably woven into the history and evolution of planets. The Earth is an example of such a planet — teeming with life, so much so that terrestrial life has completely reworked and devoured its own earlier history. It is clear that other planets have evolved differently from Earth. We need to understand the differences and why they occur. Life on Earth began between 3.5 to 4 billion years ago. During this time frame, while life on Earth was originating, the environment on Mars was warmer and wetter than at present, and it was probably more hospitable to living processes. Planets, such as Mars, may or may not have produced the appropriate organic molecules leading to life, and that life, if it arose, may or may not have survived and evolved as the planet evolved — we do not know! Only by exploration and research can we resolve the multitude of questions associated with the very profound issues of life's origin(s), evolution, and distribution.

The Planetary Protection Program, discussed in Section IV, is essential to ensure that the scientific value of Mars is protected from biological and chemical (organic) contamination from the Earth until our key scientific objectives are met. That program encompasses the development of technology to clean, and if necessary, sterilize spacecraft searching for the record of life, in order to avoid masking or even destruction of important evidence on Mars by introducing terrestrial life forms and organic molecules. The constituents most sensitive to such contamination are (if they exist):

- Indigenous life forms
- Fossil organisms
- Organic molecules.

Table III-2
Sites Within Solar System Likely to Contain Evidence of the Origin of Life*

- | | |
|---------------|----------------|
| 1. Mars | 4. Titan |
| 2. Comets | 5. Cosmic Dust |
| 3. Meteorites | |

*Approximate priority order

Approach. The search for evidence of life (extant or extinct), life related organic molecules, and water are the principal NASA objectives of a series of missions to Mars that began with the Viking missions in the mid 1970s. The search continues with a series of unmanned robotic precursor probes designed to further characterize the

chemistry of the Mars atmosphere and planetary surface, geology, seismology, and climatology. The Viking mission searched for indigenous life forms and organic molecules but found none in two small localized sites. It is important to study a far larger portion of the planet (i.e., equator to poles), in sites more representative of the variety of Mars geographies, and in sites with characteristics of particular interest from an exobiological point of view. This work can be done with orbiters, landers, and rovers which can be cleaned and sterilized so that the planet is not contaminated and future study compromised. Such a program accomplishes two things:

- We will learn much more about Mars, the solar system, and the universe so that future experiments can be better designed and more desirable sites for scientific investigation can be identified.
- We will have more confidence in the selection of human landing sites with concerns for safety and the scientific potential of the area for detailed human exploration. Human exploration will inevitably contaminate the planet; therefore, from a scientific point of view the key data concerning life should be obtained before that time.

While the likelihood of extant life on Mars is very remote, it is not zero, and the likelihood of ancient (fossil) life is much greater. Human exploration will eventually greatly facilitate the search for and study of ancient life — an undertaking which may be impossible to accomplish robotically.

Unmanned precursor missions, Moon bases, and SSF offer important opportunities for research, such as long-term cosmic dust collection for organic analysis or simulations of gas-grain interactions, which are scientific objectives of exobiology. Furthermore, Moon missions can also provide significant opportunity for exobiology science experiments, particularly those dealing with the record of chemical evolution in the early solar system.

3. Other Specifically Enabled Science

Although the Exobiology Program has been identified as uniquely enabled by Mars missions, unmanned precursor missions, Moon bases, and SSF offer exciting opportunities to conduct other life science experiments. Microgravity research will also be enabled by accelerated plant research required for long-term bioregenerative life support (CELSS) on SSF. Basic science studies of muscle physiology, cardiovascular function, vestibular and other neuroscience, regulatory physiology, and behavioral and performance studies will also be enhanced.

A Moon base that can serve as a waystation and research base for Mars missions will offer unique opportunities to conduct cellular and developmental biology experiments within the reduced gravity of the Moon. In particular, it will be of great value to assess reproduction and development (i.e., egg to egg) in this 0.16g environment compared to that in 1g centrifuges on site. In order to evaluate the impact of hypogravity on human, animal and plant systems, studies should include a variety of species over the phylogenetic range (including, but not limited to, the well understood systems of mice, insects, and roundworms). Many basic science questions included in Section III-A,

and Mars mission questions included in Sections IV, V, and VI can be addressed in Moon or Mars bases, and could provide beneficial crew activity and exciting scientific results in a Mars transit vehicle.

Cell and Developmental Biology. Questions focusing on gravity sensing responses of cellular systems and the affect of gravity on the development of anatomical structures of animals would be uniquely enabled by Moon and Mars missions.

Neuroscience. Uniquely enabled science focuses on understanding basic mechanisms of gravity perception, effects of altered gravity on changes in biological rhythms, definition of appropriate neuronal models for understanding central processing in altered gravity, and understanding how signals from different receptors are involved in orienting in altered states of gravity and motion.

Cardiopulmonary. Uniquely enabled questions focus on a basic understanding of the cardiovascular function in the microgravity environment. For example, cellular changes in the function of the heart, morphological changes involving the cardiovascular system, and understanding of pulmonary aging and pathology caused by space flight. Neuroscience studies in relation to autonomic control of cardiovascular action may be of great significance, both for spaceflight and medical treatment on Earth.

Regulatory Physiology. Further flight and ground-based investigations into the changes in the major regulatory systems of the body (the nervous, endocrine and immune systems) induced by exposure to the space environment will be required to support Mission to Planet Earth (MTPE).

Human Factors. Studies of the effect of space flight on sleep architecture, quality and quantity would be specifically enabled by long-duration Moon base studies.

Musculoskeletal. Long-duration studies facilitated by Moon and or Mars missions would help determine the effects of weight-bearing on development.

D. Educational Opportunities

The reason for voyages of discovery are tied to humankind's insatiable desire to investigate the unknown and learn. The natural fuel for learning is inquisitiveness, motivation and desire of students to learn. The spark that ignites the process is excitement. History is replete with examples of the positive benefits of exploration on technology and scientific knowledge. The Apollo Program had a dramatic impact on the development of microelectronics, materials, microminiaturization and the plethora of other "terrestrial applications" that NASA refers to by the term "spinoff." Most importantly, the Apollo Program captured the interest of a generation of Americans and motivated unprecedented numbers of young minds to pursue careers in space science and engineering.

The most critical factors in great endeavors such as MTPE and MFPE include visionary planners, committed sponsors, capable managers, daring explorers and large

numbers of dedicated, skilled, and experienced scientists and engineers. By far the most important resources are trained minds. The availability of men and women with these skills requires a nation-wide educational system that attracts and retains capable disciplined minds to the "hard sciences" and engineering fields. The current trend of fewer and fewer students, particularly ethnic minorities and women, choosing careers in these fields is alarming, is not in the best interest of NASA or the United States, and must be reversed.

NASA life sciences educational programs include the Space Life Sciences Training Program at field centers, a SETI education initiative (co-sponsored by NSF) focusing Life in the Universe as an Integrated Science Teaching Program, the Planetary Biology Intern Program, the Space Biology Research Associate Program, the Planetary Biology and Microbial Ecology Program, the Aerospace Medicine Residency Program, NASA Specialized Centers of Research and Training, and Spacelab Life Science Curriculum Supplements. These efforts should be strengthened and further integrated with the educational programs in other OSA divisions, throughout NASA, and across federal agencies. Participation with private industry and the university community must be enhanced.

The Moon and Mars missions are a unique opportunity to spark the interest of students throughout the world. The plan to get there must include resources and people dedicated to communicating both the knowledge and the excitement, thereby ushering in a new era in education.

E. Robust Program

It is impossible to address a robust science program within the bounds of robust and constrained as defined in this report. Robustness of the science program depends on the availability of flight research equipment, crew time, power, volume, etc. It also depends on a broadly based ground research program and the availability of research funds for principal investigators. It requires a spirit of openness to a diversity of hypotheses across the extraordinarily broad area called life sciences. AMAC encourages the development and implementation of a very robust science program.

IV. ENVIRONMENTAL HEALTH AND LIFE SUPPORT SYSTEMS

A. Introduction

Optimal Environmental Health and Life Support Systems (EHLSS) will protect the crew from inhospitable space and planetary environments and provide transit vehicle and planetary surface cabin environments which emulate Earth-normal conditions for those factors that directly affect crewmembers. These capabilities will alleviate the space environment causes of detrimental effects on crewmembers, thereby allowing mission performance approximately equivalent to human performance on Earth, and normal postflight lives (health and longevity).

Table IV-1 summarizes the life sustaining cabin environmental factors which must be provided by the three major support systems when humans are confined to the closed systems required for transit vehicles, planetary bases, or extra-vehicular (EVA) and extra-habitat (EHA) activities. Mission duration and maximum crew recovery time (in case of aborts) dramatically impact requirements.

TABLE IV-1 CRITICAL HABITABILITY FACTORS			
FACTORS	SYSTEMS PROVIDING CAPABILITY		
	ENVIRONMENTAL HEALTH & LIFE SUPPORT	COUNTERMEASURES	MEDICAL CARE
Food	X		C
Water	X		C
Atmosphere	X		C
Waste Management	X		
Toxicology/ Microbiology	X		C
Human Factors	X	X	C
X — Implies the potential for a solution C — Contingency capability for limited and temporary intervention or treatment			

This table is applicable to both Moon and Mars missions; however, the advantages of shorter duration missions and the capability for rapid return from the Moon will allow employment of less sophisticated systems for Moon missions.

B. Constrained Program — Early Missions Without Bioregenerative Life Support

The constrained program¹ for early Mars missions addresses critical issues in the following areas:

- Life Support Systems
- Environmental Health (barophysiology, microbiology, and toxicology)
- Behavior, Performance, and Human Factors
- Radiation Health
- Planetary Protection.

1. Food, Water, Atmosphere, and Waste Management

EHLSS with sufficient redundancy and backups to provide dependable water, food (including nutrient balance) and atmosphere (e.g., gas concentrations, temperature, humidity) are absolutely essential because countermeasures do not exist. If failure occurs, the ability of Medical Care Systems (MCS) to intervene or treat (where it is even possible) is temporary and palliative. Five critical issues (Table IV-2) focus on these life support systems.

Table IV-2
Food, Water, Atmosphere, and Waste

- • Determine requirements for human waste subsystems
- • Certify functioning and sufficiency of expendable supplies and physico-chemical regenerative technologies
- • Certify life support systems capability for providing EVA/EHA surface exploration
- • Identify food storage, processing and preparation technologies
- • Determine storage and processing requirements for potable and hygiene water

• • = Required for Moon and Mars

Research Requirements. Research is required to define the acceptable limits of quality and quantity for water, food, and atmosphere, and eventually to provide the science and technology necessary to develop sustainable regenerative (biological and/or physico-chemical) life support systems.

2. Environmental Health

Maintaining humans in confined systems presents a unique challenge, which is exacerbated by extended mission duration, for toxicological and microbiological management issues. Adequate redundancy and backup must be included because optimized MCS (e.g., treatment with antibiotics, drugs) are palliative and can only be utilized for relatively short periods to assure crew mission performance and recovery.

Footnote 1. 17% of the critical questions identified in the discipline plans support a constrained EHLSS program (see Volume II, Table 2).

Critical issues (Table IV-3) focus on microbial contamination and materials (e.g., chemicals, biologicals, and particulates), atmospheric composition, and pressure anomalies that might adversely affect crew health and performance. Environmental standards need to be developed for chronic conditions involving the long-duration of a Mars mission. Monitoring strategies and procedures must be developed for determining which components of the spacecraft internal environment or planetary habitat must be monitored to adequately assess environmental safety, particularly what contaminants are likely to build-up over the long-duration in a closed environment. Sample types, numbers, and sampling frequency, as well as data analysis, must be identified.

**Table IV-3
Environmental Health**

- Establish standards for number and kinds of organisms in water, air, food and on surfaces
- Identify crew health, safety, and performance effects of chronic exposure to respirable and nonrespirable particles
- Identify effects of atmospheric components on crew physical and psychological well-being
- Identify effects on crew physiological responses of interactions between microgravity and off-baseline atmospheric composition, pressure, and temperature
- Determine impact of flight-induced physiological responses on crewmember susceptibility to toxic materials, microorganisms, and environmental contaminants
- Develop reliable approaches for predicting acceptable exposure levels from limited data
- Assess available technology for identifying microorganisms in crew and environmental specimens and how antimicrobial procedures control microorganisms in space
- Develop real-time systems for monitoring air quality
- Predict (utilizing traditional time exposure and human toxicological data) acceptable values for inhalation and ingestion exposures to chemicals in space flight
- Determine effects of space flight on microbes

•• = Required for Moon and Mars

Research Requirements. Ground-based research and space flight experience have established a scientific basis for defining standards for air and waterborne gaseous and particulate microorganisms, and atmospheric composition and pressure. However, information regarding their long-term effects on crew performance and health is insufficient. Enhanced capability (i.e., advanced sensors) for real-time environmental monitoring systems is required to support a Mars mission. Additional research is needed to develop technology for environmental control and monitoring systems for gas composition, pressure, temperature, and humidity. This research and development is required for the cabin environment of planetary bases, spacesuits and transit vehicles.

Human exploration missions will require establishment of standards for the number and kinds of microorganisms in air, water, food, and on surfaces within the spacecraft cabin or planetary habitat. Assessments of the presently accepted or proposed standards, such as the spacecraft maximum allowable concentration (SMAC) values for toxicants, and the maximum allowable counts of microorganisms need to be conducted. Validating the applicability in space of Environmental Protection Agency

(EPA) potable water standards, and EPA and Food and Drug Administration (FDA) standards for food is a necessary step in defining standards for exploration missions.

EVA will be part of any exploration mission scenario, either as a planned activity or in an emergency during transit. Therefore, issues involving the prevention of decompression sickness and acceptable risks for conducting EVA (e.g., venous gas bubbles, bends, Central Nervous System (CNS) effects, and cardiovascular symptoms) must be fully understood. Ground-based research must continue or be accelerated, and flight validation during extended Spacelab missions, on SSF, and at the Moon outpost, will be required before a Mars mission.

3. Behavior, Performance, and Human Factors

For the early Mars mission, critical EHLSS issues (Table IV-4) in habitability and human factors focus on problems involving habitability requirements for transit spacecraft and planetary habitats and human-machine interfaces. Research and technology development for habitability requirements and human-machine interfaces will provide designs that maximize productivity and minimize occupational injuries. MCS, in a manner analogous to Earth operations, will be utilized to treat occupational illness and injuries.

Table IV-4
Human Factors and Habitability Issues

- Determine requirements for habitability (e.g., lighting, work/rest schedule) to maximize performance
 - Determine optimum allocation of functions, including operator discretion, between humans and machines to maximize maintainability and reliability
 - Determine behavioral correlates of space-induced physiological changes
- = Required for Moon and Mars

The habitable volume and crew size limitations for transit vehicles and planetary bases, only allow EHLSS that partially provide (e.g., by habitat design) near Earth-normal conditions for factors that impact mental health. However, countermeasures (e.g., crew selection, planned activities, work/rest cycles) may sustain mental health which approaches Earth-normal, allowing acceptable mission performance and postflight recovery. If countermeasures are insufficient and crew mental health and morale degrades, MCS will play only a limited role.

Data on performance assessment and mental workload during missions are limited in scope in areas of task analysis (e.g., experiment errors, lost data, and equipment mishandling due to human-machine interface problems). Some inflight evaluations of workstation design are being performed on Space Shuttle flights to identify the most effective design for utilization in space. Procedures for allocating functions between humans and machines must be developed before embarking on long-duration missions.

Spacecraft habitability problems (e.g., high noise levels and unpleasant odors) have been reported during short-duration space flight. Limited observational data from

Space Shuttle missions (e.g., crews perceive the living space as confined, food as restricted in quality and diversity, lack of privacy and personal hygiene facilities) suggest that significantly improved habitability will be essential for maintaining crew mental health and performance on long-duration missions.

Research Requirements. Ground-based research, aviation research and operational experience, and data from isolated and confined settings have yielded information regarding human performance and productivity. The applicability of this extensive knowledge base for behavior, performance, and human factors designs for operations in long-duration space flight must be thoroughly examined.

A recent report by the National Research Council Space Studies Board (1991) emphasizes the importance of conducting ground-based studies in a variety of research settings in order to understand group performance and functioning. It is their recommendation that studies involve confined groups for three to four years. It is also important to validate the results from analog settings involving laboratories and field experiments (e.g., Antarctic analog) in operational environments (i.e., Spacelabs, SSF, and Moon base).

4. Planetary Protection

Because Mars is potentially hospitable to life, missions to this planet provide an exciting and unique opportunity to increase our knowledge of the origin, evolution, and distribution of life in the universe. Contamination from Earth would obfuscate evidence concerning chemical-biological evolution and the existence of hypothesized extinct and extant species. A planetary protection program is required to protect Mars from biological and chemical contamination as well as to protect Earth from importation of biological materials from Mars.

Requirements and procedures to prevent forward contamination demonstrated on Viking missions must be refined for Mars missions. Policies, procedures, equipment, and facilities to protect against back contamination are less developed (Table IV-5).

Table IV-5
Planetary Protection

- Establish improved requirements to protect Mars from Earth contamination applicable to robotic precursors and human missions (forward contamination)
- Establish requirements for robotic and human exploration to protect the Earth from biological contamination from Mars (back contamination)
- = Required for Mars

Research Requirements. Technology development efforts required to support planetary protection include development of: (1) alternative sterilization methods (e.g., alternatives to dry heat sterilization); (2) remote sealing, verification and monitoring technologies; (3) aseptic transfer technologies; (4) developmental risk analysis methods; and (5) containment technology and appropriate quarantine protocols for the receiving labs on Earth. Robotic missions prior to manned exploration are mandatory. In conjunction with early sample return, plans must be initiated for an Earth-based

Mars sample quarantine (containment and analysis) facility in which samples will be isolated and analyzed. There is a need to form an interagency committee for jurisdiction over planetary protection concerns.

C. Constrained Program - Human Operations in the Radiation Environment of Space

Low level radiation poses a significant health hazard, that becomes more severe with extended exposure duration. Duration of exposure and levels of radiation within transit vehicle and planetary base habitats vary with mission scenario, thereby posing unique mission dependent challenges for design of crew support systems (see Table IV-6).

TABLE IV-6 MISSION SCENARIO SENSITIVE ENVIRONMENTAL FACTORS — RADIATION			
MISSION SCENARIOS	SYSTEMS PROVIDING CAPABILITY		
	ENVIRONMENTAL HEALTH & LIFE SUPPORT	COUNTER- MEASURES* *	MEDICAL CARE
(1) Transit Vehicles			
• Mars Missions	X		C
• Moon Missions	X*		C
• EVA	X*		C
(2) Planetary Surfaces			
• Base			
Mars	X		C
Moon	X		C
• EVA			
Mars	X*		C
Moon	X*		C
* — Solar event prediction required * * — Protectants for radiation exposure X — Implies the potential for a solution C — Contingency capability for limited and temporary intervention or treatment			

There are neither countermeasures nor totally effective medical treatments for humans exposed to radiation, therefore EHLSS shields are the only means of protecting humans for extended durations in transit or on planetary surfaces. The capability to provide sufficient warning of large solar events should allow unshielded Moon transit; Moon and Mars EVA; and Mars transit vehicles that incorporate shielded sanctuaries.

Similarly a solar event warning capability would enable EHA on planetary surfaces and sanctuary architectures for bases. Shielding with regolith may provide acceptable radiation levels throughout human habitats in planetary bases. Currently, information

necessary to quantify health hazards and design effective shielding from HZE is based on empirical models.

The radiation environment of space external to Earth's atmosphere is so hostile to life as we know it that there can be no compromises, and the issues (Table IV-7) must be addressed in the constrained program.

Table IV-7
Radiation Health

- • Determine the interplanetary radiation environment for:
 - • Galactic cosmic radiation (GCR) as a function of partial energy, linear energy transfer (LET) and solar cycle for mission profiles
 - • Maximum flux, integrated fluence, and the probability of large solar particle events (SPE) during any mission
 - • Determine the internal space radiation environment of space vehicles
 - • Develop improved protection from GCR and SPE (proton radiation)
 - • Determine how a radiation field is transformed as a function of depth of different materials
 - • Determine doses related to heavy ions and solar particle flux in deep space
 - • Determine the particle multiplicities of nuclear radiation products
 - • Quantify the biological effects of GCR and proton radiation from SPE
 - • Determine the interaction effects of radiation and hypogravity
 - • Validate ground-based research in space
- • = Required for Moon and Mars

Research Requirements. Required research includes:

- Characterization of radiation environments in transit vehicles
- Determination of the radiation effects of protons and heavy ions on biological systems
- Determination of the risks of stochastic effects (i.e., cancer and genetic) and acute deterministic effects (e.g., damage to rapid cell renewal systems in bone marrow, gut and skin), and late deterministic effects (e.g., cataracts and CNS damage)
- Development of methods (e.g., pharmacological agents and bone marrow preservation) for protecting against:
 - Acute effects that might occur with a very large SPE
 - Late effects (in particular cancer) from HZE and proton exposure.

It is critical for NASA to formalize agreements to utilize one or more of the federal accelerator facilities, and to assure that those facilities remain in operation until necessary ground-based research is completed.

In order to develop effective radiation protection, Moon orbiters and rovers must include the capability to quantify GCR and SPE proton levels. They must also include the means to evaluate potential radiation shielding and accommodate experiments to determine biological effects from HZE and SPE exposure.

The primary research thrust should be in prevention of exposure to the maximum extent possible since countermeasures or treatments are not sufficiently developed and might not yield solutions by the time exploration missions are initiated.

D. Constrained Program — Later Missions With Bioregenerative Life Support

The volume and mass of stowage necessary to support crews increases with mission duration and crew size; therefore, hybrid and/or bioregenerative systems will become essential for later Mars missions. The primary difference between "early mission" and "late mission" constrained programs is the exclusion of bioregenerative life support systems from early mission scenarios. If ongoing research programs produce technological breakthroughs in bioregenerative systems or physico-chemical systems meet unforeseen difficulties, it might be feasible and beneficial to use the former in earlier exploration missions.

The constrained program for later Mars missions (i.e., with bioregenerative life support systems) addresses critical issues in the following life sciences areas:

- Life Support Systems
- Plant Biology
- Cell and Developmental Biology
- Radiation Biology.

1. Life Support Systems

Life support designs for Skylab, the Space Shuttle, SSF, and Mir (if one excludes fresh vegetables grown periodically on Soviet missions) are based on stowage of materials before launch and resupply. This has been adequate for short-term Earth orbital and short-duration Moon missions.

Regenerative life support systems based solely on physico-chemical (PC) technologies being developed for SSF and human exploration missions, cannot regenerate food from waste. Eventually, the operational system must include biologically based components utilizing green-plant photosynthesis capable of generating food, oxygen, and potable water, removing carbon dioxide, and using microbial degradation and mineralization of waste. SSF provides an opportunity to develop, test, and gradually introduce regenerative technologies, particularly for water and air, to reduce transportation burdens.

The fundamental strategy of the Controlled Ecological Life Support System (CELSS) Program is to emulate the life-sustaining processes of Earth. However, because of constraints on volume, mass, energy, and crew time, integrated bioregenerative — PC systems will undoubtedly be the most practical for late missions.

Present understanding of the size, volume, and energy required for a total CELSS suggests that for mission lengths of 600- to 1000- days, such systems would not provide significant savings over PC life support systems. However, some fresh food derived from plants may be desirable for nutritional and psychological reasons. For

example, Soviet experiences with long duration Mir missions indicate that the presence of living plants and the availability of fresh foods have enormous positive impact on crew psychological well-being and work capacity.

Research Requirements. The major issues (Table IV-8) associated with PC air regeneration include replacement of consumed oxygen, removal of carbon dioxide, and reduction of the amounts of volatile organics and particulates. Major issues associated with PC water regeneration include identification of particulates and solutes in waste water streams that must be processed, establishment of realistic requirements for the product (purified water), evaluation of potential methods of solute removal, and maintenance of long-term water quality in a dynamic recycling system. Issues associated with solid waste stabilization include reduction of volume, containment and removal of off-gases; containment or neutralization of pathogenic organisms; and storage.

Table IV-8
Life Support Systems

Physico-Chemical

- • Determine best technologies for recycling potable and hygiene water
- • Determine effects of the space environment on microbial interactions with space systems (especially bioregenerative) and humans
- • Evaluate and select strategies and techniques to control causes of life support system instability
- • Evaluate use of mathematical models in system design, simulation, and systems operations
- • Determine specific caloric, fluid, macronutrient, fiber, and micronutrient requirements
- • Develop prioritized acceptability criteria for foods

Bioregenerative

- • Assess CELSS instabilities due to limited volume and intense dynamics
- • Determine CELSS produced foods to satisfy acceptability criteria
- • Evaluate extent to which microorganisms in a physico-chemical waste processor may degrade CELSS performance
- • Establish CELSS system design and operation requirements considering redundancy, subsystem failures, monitoring and control technologies, interaction between bioregenerative and physico-chemical subsystems
- • Determine sensors required to automate CELSS
- • Determine available air treatment technologies, CELSS utilization, and development of technologies for space application
- • Determine acceptable thresholds for revitalized air in an operational CELSS
- • Determine conditions required for optimizing food generation and water recycling of crop plants
- • Determine whether extraterrestrially grown crop plants can produce sufficient edible biomass to support humans

• • = Required for Moon and Mars

Human acceptance, nutritional standards, and processing and storage requirements for food were assessed at the highest levels of criticality for research for a Mars mission. It is highly likely that fresh foods derived from plants will be required for

extended missions. Many of the high-priority research issues for CELSS development (e.g., storage requirements for potable water and control of microbial films) are also required for pure PC systems (Table IV-8). This life support research is also important to developing technologies essential for environmental health of humans in space.

Investigations must include the possibility that fresh foods, particularly plant-derived foods, will be required to enhance crew morale and mental health and prevent nutritional deficiencies. Such deficiencies could be due to inadequacy of the diet, flight-related changes in nutritional requirements, or crew appetites on long-duration missions.

It is crucial that basic studies be conducted to determine whether safe and sufficient supplies of water, air, and food can be provided by current or developing expendable systems within presently understood constraints of spacecraft storage capacity, crew size, and mission duration. Trade-off studies comparing expendable systems with even partial recycling of water and air using biological systems have the highest priority for research and development in the CELSS Program.

Research on photosynthetic productivity should be cooperatively developed with National Science Foundation (NSF) and United States Department of Agriculture (USDA). Research on waste recycling and food processing should be cooperatively developed with Department of Energy (DOE), USDA, National Institutes of Health (NIH), NSF, EPA, and FDA.

2. Plant Biology

A knowledge of plant gravitational biology (particularly in microgravity and at Moon and Mars gravity levels) is integral to implementation and operation of a bioregenerative life support system in space. Specifically, basic information about plant gravity thresholds and the effects of gravity on nutrition, growth, differentiation, reproduction, metabolism, and photosynthesis provides the fundamental basis for such a system. Therefore, the criticality of these research issues (Table IV-9) in support of exploration missions is directly related to decisions to incorporate a plant-based bioregenerative life support system.

Research Requirements. The United States has had a moderately funded ground-based plant biology program for the past 15 years, and the flight program has been far from robust. As a result, many critical issues pertaining to plant gravitational biology have not been answered, and many life support scientists in the CELSS Program require answers to the same scientific questions as do scientists concerned with more basic questions. For example, what is the gravitational threshold for normal and productive plant growth and development? Can plants go from seed-to-seed-to-seed in the space flight environment? How are crop frequency and size affected by microgravity or other space-related environmental influences? As a result, there is considerable overlap between CELSS and plant space biology.

Many of the plant biology issues assessed as criticality 2 may become criticality 1 if ongoing space-based research reveals additional problems with plant development

and physiology and if bioregenerative life support is required during early manned missions.

**Table IV-9
Plant Biology**

- • Determine whether plants can reproduce through multiple generations in space or on the Moon or Mars
 - • Determine microgravity and other space-factor effects on single cell or higher plants growth rates; differentiation; anabolic, catabolic and photosynthetic pathways or apparatus; nutrient absorption pathways; support polymer synthesis; chromosomal integrity and behavior during cell division; water transport; transpiration; embryogenesis and life cycle stages in plants.
 - • Determine the threshold levels for gravity effects
 - • Identify perception and response to microgravity differences between species and between tissues
- Determine interaction effects between radiation, environmental factors and microgravity on development of botanical systems

• • = Required for Moon and Mars

3. Cell and Developmental Biology

Space flight experiments to date have not demonstrated debilitating cellular effects from exposure to the space flight environment. However, since inflight experiments have been limited, there is insufficient evidence to draw definitive conclusions. The primary issue (Table IV-10) in cell biology is the requirement to obtain such evidence from a well-controlled flight science program.

**Table IV-10
Cell and Developmental Biology**

- • Determine microgravity effects on cells and the influence of magnetic fields and radiation
- Determine low dose radiation and lowered gravity effects on male and female germ cells
 - What events in gametogenesis and early germ maturation are gravity sensitive and how can these results relate to proliferation and differentiation of other individual cell types?
 - Can altered gravities affect fertilization and do these results indicate more general mechanisms of membrane alteration in individual cells?
 - Which responses are transmitted maternally and which are intrinsic to the developing embryo?
 - How do altered gravity levels effect axis polarity and asymmetries of zygotes?
 - Are there gravity or other environmental effects that can cause change in gene activation, transcription or translation?

• = Required for Mars

• • = Required for Moon and Mars

E. Robust Program

The robust program for EHLSS would include the following elements:

- An expanded basic research program
 - Accelerated research by expanding the number of principal investigators (PIs) and the diversity of approaches
- An enriched radiation protection program
 - A series of dedicated retrievable biosatellites to collect HZE-based radiation data, including multigenerational data on different species
 - Characterization of solar cycle dependence of space radiation, trapped radiation flux, and energy spectra of electrons
 - Determination of probabilities for GCR-related damage
 - Characterization of mechanisms involved in modulating damage, including utilization of animal models to extrapolate human radiation risks, such as probabilities for different radiobiological outcomes (e.g., cataracts, detrimental genetic development); and utilization of cellular mechanisms to understand whole organism effects
- An expanded life support program
 - Development of life support systems that provide food production for transit vehicles and planetary bases
 - Development of highly automated systems designed with advanced sensors (e.g., immobilized bioactive molecules) and controls that can respond to toxicological and microbiological contamination events
 - Accelerated development of processes to convert non-edible plant waste to edible food ingredients
 - Development and application of genetic engineering
- Accelerated programs to optimize cost-effective design solutions for habitability and performance
 - Sophisticated models and simulators that have the highest fidelity that is technically feasible to establish cost effective design solutions to human factors issues, such as behaviorally and ergonomically-designed systems for providing better habitation and human-machine interfaces
 - Refined anthropometric standards and automated systems for crew communication and training
- An enhanced space physiology program
 - Additional studies to understand physiological and other responses under different atmospheric pressures and compositions, including combustion/flammability, particle deposition and evolution
 - Expanded studies of space flight environmental conditions that influence regulation of temperature, fluids and electrolytes
 - Studies to identify biomarkers for detection of human exposure to contamination
- An accelerated program to develop engineering requirements and determine biological consequences for artificial gravity engineering (e.g., tethers, rotating spacecraft and short-armed or long-radius centrifuges)

- Development of enhanced waste treatment and biological containment systems to delay contamination of Mars and extend the window of opportunity for exobiology studies of Mars.

F. Requirements for Moon Exploration Missions

Because of the relatively short Moon recovery times and mission durations, Moon EHLSS facilities, equipment, and procedures can evolutionarily build in complexity from SSF capabilities until they allow a full scale operational test of Mars mission capabilities. As indicated in the boxed lists in the previous discussion, the only issues for Mars missions that are not required for Moon missions are: (1) planetary protection; and (2) effects of continuous long-duration radiation exposure.

V. COUNTERMEASURE SYSTEMS

A. Introduction

Countermeasures Systems (CS) compensate for the detrimental effects of the space environment on crewmembers. While EHLSS systems prevent the space environment from degrading the crews' health status by providing or emulating Earth-normal cabin conditions (e.g. normal temperature, pressure, gas concentration, shields to minimize radiation from reaching the crew, and artificial 1g transit vehicles), CS must compensate for the fact that the crewmember is directly exposed to a hazardous environment. There are three types of CS: (1) those that depend upon preflight selection criteria; (2) those that prevent adaptive responses to microgravity and other space flight environment factors and therefore are prescribed throughout the mission (e.g., intermittent artificial gravity); and (3) those that restore or correct a deficit that only becomes evident during transition to a new g field (e.g., landing on Mars or return to Earth) and would be administered just before and/or after the transition. Ideally, CS will prophylactically intervene to prevent illness, injury, and pathophysiology that would result in behavioral and performance degradation. Countermeasure Systems must provide acceptable mission performance and postflight recovery when: (1) EHLSS cannot provide nominally Earth-normal environmental conditions for crews because science or technology are not available, or where cost and schedule limitations prohibit them; or (2) EHLSS fail, but only for short periods. Critical questions¹ in life sciences that support a constrained research and development program for CS are detailed in Volume II.

B. Constrained Program — Countermeasures for Crew Exposure to Hypogravity

U.S. and Soviet flight experiments, ground-based research, and operational flight experience have identified detrimental effects on human health and performance in microgravity on short-duration missions, even though currently available countermeasures are used. Generally, undesirable effects become more severe with extended exposure duration. Duration of exposure and levels of gravity within transit vehicles and in planetary base habitats are directly related to specific mission scenarios. Likewise, the impact on crew physiology, mission performance, and postflight recovery are mission specific (Table V-1).

The requirements for countermeasures become more complex as NASA advances from Spacelabs to SSF to Moon and Mars missions of increasingly extended duration with multiple gravity levels (Table V-2).

Although improved capability is desirable, the Apollo Program demonstrated the ability for crews to successfully perform short-duration Moon mission tasks during microgravity transit EVA and surface (0.16g) EHA. Gravity thresholds for biological processes have not been determined. Therefore, the impact of extended duration exposure to 0.16g on the Moon surface is unknown. Consequently, the requirements for countermeasures in long-duration Moon bases cannot be fully defined.

Footnote 1. 11.5% of the criticality 1 and 2 questions support a constrained CS program (Volume II, Table 2).

TABLE V-1 PROTECTION AGAINST HYPOGRAVITY EFFECTS			
MISSION SCENARIOS	SYSTEMS PROVIDING CAPABILITY		
	ENVIRONMENTAL HEALTH & LIFE SUPPORT	COUNTER- MEASURES*	MEDICAL CARE
(1) Transit Vehicles • Mars Missions • Moon Missions • EVA	X*	X*	C C C
(2) Planetary Surfaces • Base Mars Moon • EHA Mars Moon	TBD TBD	X X	C C C C
* — May include artificial gravity X — Implies the potential for a solution C — Contingency capability for limited and temporary intervention or treatment TBD — Indicates uncertainty about system requirements at 0.16g and 0.38g			

Data from U.S. and Soviet space flights dictate a critical requirement for improved countermeasures in microgravity transit vehicles. The known detrimental effects of microgravity, and the absence of biological threshold data or specific data on living systems under Mars (0.38g) gravitational conditions make it prudent to plan for countermeasures at a Mars base even in the shortest (<30 day) scenarios. Human centrifuges could be technologically and programmatically feasible as countermeasures for decreased gravity within planetary bases or a Mars transit vehicle. However, scientific evidence on the merit of intermittent gravity loading under these conditions is needed.

The microgravity countermeasures research plan encompasses activities necessary to establish the strategies for developing, testing, and validating the efficacy of procedures, tools, models, and systems necessary to maintain health and performance. This report addresses the most complex case (microgravity Mars transit and effects of 0.16g and 0.38g are assumed to be as serious as microgravity) and assumes that hypogravity countermeasures will be required during Mars transit and Moon and Mars surface activities.

The constrained countermeasures program against hypogravity effects contains critical issues from the following life sciences disciplines:

- Musculoskeletal
- Neuroscience
- Cardiopulmonary
- Regulatory Physiology
- Cell and Developmental.

Table V-2
Microgravity Countermeasure Requirements

Spacelabs

Current Capabilities ≤16 days μ g

SSF

Orbiter*	30 day μ g
Orbiter*	60 day μ g
Orbiter*	90 day μ g
Station	90 -? day μ g

Moon

Visit	
Orbiter crew:	< 20 days μ g
Surface crew:	≈14 days 0.16g Plus several days μ g

Outpost

Orbiter crew:	? days μ g
Surface crew:	40-180 days 0.16g Plus several days μ g

Settlement

Orbiter crew:	? days μ g
Surface crew:	360-600 days 0.16g Plus several days μ g

Mars Simulation

Moon orbiter:	120-460 days μ g
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Mars (without artificial gravity)

Visit	
Orbiter crew:	600-1000 days μ g
Surface crew:	
Transit	? days μ g
Surface	30-100 days 0.38g
Transit	? days μ g

Outpost

Orbiter crew:	≈1500 days μ g
Surface crew:	
Transit	? days μ g
Surface	≈600 days 0.38g
Transit	? days μ g

* Options being studied

Countermeasure procedures are currently being developed, utilized, and evaluated in both the U.S. and Russian space programs. The normal sequence of adaptive physiological events, normal variability between individuals, and the interaction

among individual countermeasures confound evaluation of their effectiveness. Current countermeasures include:

- Pharmacological (anti-motion sickness, anti-orthostatic intolerance and anti-bone loss drugs)
- Exercise (treadmill, cycle ergometer and resistance exercise; isometric, isokinetic, isotonic and concentric protocols)
- Dietary (fluid loading, mineral and/or metabolic supplements)
- Environmental (lighting, oxygen pre-breathing)
- Mechanical (lower body negative pressure, gravity suit)
- Psychological (ground support, biofeedback)
- Special training (preflight adaptation trainer, skill maintenance).

Crews in Mars transit vehicles with EHLSS systems that may incorporate artificial gravity should experience near Earth-normal conditions. This may be helpful in transit and on return to Earth. Chronic exposure to coriolis forces necessary to create artificial gravity will have to be studied. The physiological response to transition between the vehicle providing artificial gravity and the Mars surface (0.38g) during arrival and departure are unknown. Extensive U.S and Soviet EVA experience suggests that microgravity effects for EVA or transition to Mars gravity from transit vehicles (with 1g artificial) will not require EHLSS or CS. But the deconditioning resulting from stopping the rotation (for 1g artificial) of the transit vehicle may affect performance during and after Mars landing. The physiological and behavioral consequences of repeated, planned or emergency EVAs from a 1g transit vehicle are also unknown.

1. Musculoskeletal

The extensive list of issues (Table V-3) related to musculoskeletal systems reflects: (1) extensive evidence of detrimental effects from U.S. and Soviet space flight; (2) the results of relatively robust flight and ground-based musculoskeletal research programs; and (3) evidence that, without countermeasures, crews are likely to suffer mission limiting (or terminating) injury or illness and/or irreversible damage from a long duration Mars mission.

Table V-3
Musculoskeletal

- Determine regulation of muscle metabolism during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading
- • Determine the endocrine and nutritional requirements to maintain bone, muscle, and connective tissue, the interaction with mechanical loading and the effects induced by space flight
- • Determine whether bone loss is reversible in terms of mass, ultra- and microstructural organization
 - Extent to which irreversible adaptations in bone architecture affect structural integrity
- Identify bone and connective tissue markers or metabolism
 - = Required for Mars
 - • = Required for Moon and Mars

In muscle the primary effect of adaptations to space flight appears to be a loss of contractile protein in the muscle fibers. This translates to a loss in the cross-sectional area of muscle fibers which is proportional to the loss of force potential. The extent of loss remains undefined. The loss in cross-sectional area reflects a general loss of muscle mass. Although there are subsequent and even simultaneous adaptations in the type of contractile protein (e.g., types of myosin) expressed by some fibers, the principal adaptation of physiological significance seems to be the loss of contractile protein.

Connective tissue (bone and soft tissue) function is also affected by space flight. However, the precise effect and time course of changes in connective tissue is not as clearly defined as those in skeletal muscle. It is known that bone growth is inhibited in growing rats during space flight. In older rats bone length is unaffected by short flights (i.e., up to 2 weeks) but some structural remodeling may occur. The effects of space flight on other connective tissue, such as those which contribute to the extra fiber space in skeletal muscle and the tendonous component of muscle and ligaments of a joint remains undefined. Although much less is known about soft connective tissues, initial indications are that they are highly affected by unloading during rat tail suspension, human bedrest studies, and space flight.

The functional significance of these changes lies in the high probability that muscle atrophied because of space flight, if suddenly required to be active, may be particularly susceptible to injury at one or more attachment interfaces between the contractile elements of muscle and the connective tissue that transmits forces to the bones. To develop countermeasures for muscle atrophy, understanding of the mechanisms by which the space flight environment induces muscle atrophy must be significantly improved.

There is clear evidence that forces transmitted by or to musculoskeletal tissues play a modulatory role in the adaptation of bone to space flight and the effectiveness of countermeasures. It is equally clear that some hormones can influence both the kind of proteins expressed (e.g., slow or fast myosin) and the amount of protein. Further, it is becoming increasingly obvious that musculoskeletal tissues may be affected by growth factors. In establishing countermeasure strategies to maintain musculoskeletal homeostasis, it is important to consider that previous research has not been successful in fully preventing atrophy of this system using conditioning paradigms predicated on low force, high frequency activities (i.e., aerobic treadmill and cycling).

Research Requirements. Based on current information, one key goal is to develop countermeasures to the known adaptative changes in space flight that lead to impaired function. Specifically, efforts must be made to define the force patterns of specific types of muscles and bones during routine activities over the microgravity to 1g range to determine the role these forces play in maintaining structure and function of muscle, connective tissue, and bone.

Research efforts to define the role of growth factors in modulating musculoskeletal proteins during growth and development, and during adaptations to the space environment, are equally important. The primary goal for programmatic development of efficacious countermeasures for musculoskeletal function in prolonged spaceflight is to identify factors that influence musculoskeletal protein synthesis and degradation, and its assembly and disassembly as organized intercellular and extracellular and

transmembrane functional units (e.g., sarcomeres). A fundamental scientific understanding, which includes the sequence of physiological and molecular events that lead to protein modulation, will provide the basis for selecting effective countermeasures for a variety of functionally unique musculoskeletal units (e.g., flexors vs. extensors, or arms vs. legs).

Since heavy resistance exercise (i.e., high force, low frequency) has been shown to induce muscle hypertrophy in both human and animal subjects, it is reasonable to more extensively explore high force, low frequency countermeasures. It is important to examine: 1) different activity paradigms in combination; 2) the combination of activity and pharmacological and hormonal interventions; and 3) the interaction of activity and intermittent exposure to gravitational loads.

Development of effective measures to prevent, limit, or counter bone loss will require research to: (1) identify the sites, time course, and magnitude of bone loss in microgravity, 0.16g and 0.38g; (2) understand the interactions with other body systems (e.g. endocrine), other space flight factors (e.g., nutrition and circulation rhythms), and countermeasures for other adaptations (e.g., mechanical loading and exercise countermeasure for hypogravity; (3) characterize bone recovery on planetary surfaces (0.16g, 0.38g and 1g); (4) quantify the risk of fractures; and (5) develop countermeasures. It is essential to understand the effects of space flight on the mechanisms which control changes in bones (e.g., balance of osteoblastic and osteoclastic activity, perfusion dynamics, changes in serum calcium balance) in both males and females. The impact of the space flight environment on bone fracture healing is unknown.

2. Cardiopulmonary

The potential for cardiovascular problems is well known from U.S. and Soviet space flights. Cardiovascular difficulties include orthostatic intolerance, headward shift of body fluids, reduction in aerobic capacity and musculoskeletal weakening associated with fluid and electrolyte changes (Table V-3). Various countermeasures for these problems have been implemented both in the United States and Russia, but none has been fully successful. Weakness and orthostatic intolerance pose potential operational hazards during transition to Moon, Mars, or Earth gravity fields, or emergencies during flight.

Table V-4
Cardiovascular

- Determine relationship (and threshold) between electrical and mechanical (cardiac output and reserve) cardiovascular responses and exposure to various gravity levels (force, frequency and time interval)
- • Determine most effective countermeasures to avert adverse cardiovascular effects for both long- and short-duration missions and how they should be applied
 - = Required for Mars
 - • = Required for Moon and Mars

Less is known about the stability of electrical activity of the heart. There is evidence of electrical instability (e.g., arrhythmias) during EVA and during Moon exploration. It is not known whether arrhythmia is part of the orthostatic intolerance syndrome, or more

importantly, whether the stress of prolonged weightlessness, increases the occurrence of arrhythmias and reduces mechanical efficiency of the heart. The cardiovascular and pulmonary (e.g., ventilation and respiration) effects of crew exposure to toxins and radiation pose a completely unexplored threat.

Research Requirements. Integrated physiology research programs involving each body system function must address beneficial and detrimental adaptations. Careful study of neurovascular and cardiac responses must continue, and include histological and morphometric (e.g., electron microscopic) studies of small vessels and neural structures. Comprehensive investigations, on Earth and in microgravity, of intracellular and intercellular processes, including elucidation of myocardial cellular and molecular biology, is a promising approach to develop optimal countermeasures. Many of these issues could be clarified by low Earth orbit (e.g., Space Shuttle, SSF) experiments on animals.

3. Regulatory Physiology

Regulatory physiology is central to research programs involving any individual body system and must be incorporated into all investigations aimed at understanding adaptation processes and countermeasures.

The physiology of humans is composed of a totally integrated set of complex subsystems that: (1) adapt to changes in their internal and external environments; and (2) maintain critical physiological parameters (e.g., temperature, fluid and electrolyte levels) at relatively stable levels (i.e., homeostasis). Operational observations and space flight experiments have demonstrated changes in a wide diversity of these physiological parameters and processes. We do not know which of these changes are simply adjustments to a new homeostatic equilibrium (analogous to changes that occur when humans change diets, altitudes, climates, etc., on Earth) appropriate for the hypogravity environment (i.e., what is "normal" in hypogravity) and therefore do not require countermeasures (in fact countermeasures during space flight could be detrimental). Nor do we know which are life or performance threatening changes that must be ameliorated. It is clear that hypogravity countermeasures must consist of integrated approaches that encompass the complete set of human subsystems, and they must be evaluated for beneficial and detrimental effects (Table V-4).

a. Endocrinology

The transmission of information in the body and its integration across subsystems depends on integrated central nervous system (CNS) and endocrine (neurohumoral, neuroendocrine) communication systems. Recent endocrinology studies of diffuse and extensive control mechanisms outside the CNS (e.g., kidney, gut) have demonstrated widespread regulatory effects. Endocrine and neuroendocrine secretions play an extensive modulatory role, and are the basis for developing and sustaining regulatory changes throughout the body.

Measurement of changes in hormonal synthesis, release, and target cell or organ response during space flight is essential to understanding adaptation to this new environment. Understanding the effect of space flight-induced changes in hormones on the brain is key to homeostatic regulation of physiological processes (e.g., body

Table V-5
Regulatory Physiology

- Determine effects of space flight on sleep cycles and regulation of circadian rhythms and their impact on physiological adaptation, response to stress and performance and develop countermeasure systems accordingly
 - Determine how adaptive responses to space flight effect absorption, potency, toxicity and side effects of hormones and medications
 - Determine effects of extended missions on kidney functions, especially filtration, reabsorption, secretion and excretion (e.g., fluid and electrolyte losses, kidney stones)
 - Determine effects of prolonged space flight, EVA, and countermeasures on thirst, sweating, appetite and body temperature regulation
 - Determine nature, time course, and severity of immune function changes in space flight and which factors are responsible
 - Determine how space flight factors affect nutritional requirements and gastrointestinal function (e.g., absorption, motility, secretion)
- = Required for Mars

temperature, fluid balance, biological rhythms) and is central to understanding the role of gravity in: (1) the evolution and regulation of living systems, and (2) physiological and behavioral (e.g., emotional state, performance) changes that occur in humans during space flight.

Although data regarding the detailed responses of the neuroendocrine system to extended space flight are limited, it is clear that countermeasures to stabilize endocrine levels are required. Furthermore, pharmacological and behavioral manipulation of the endocrine system is an attractive avenue for introducing countermeasures for other space flight adaptations.

Research Requirements. The changes in hormone levels, receptor activity, and hormone action during space flight and re-exposure to a gravitational and other space flight environment must be understood and countermeasures for detrimental adaptations must be developed. Research to understand the effects of space flight induced endocrine system changes on the function of other homeostatic systems (e.g., cardiovascular, immune, musculoskeletal, and central nervous system) is key to understanding adaptations to space flight, and developing countermeasures for those systems.

b. Fluid and Electrolyte Balance

Mechanisms leading to the acute loss of fluid and electrolytes observed during the initial phase of adaptation to microgravity during U.S. and Soviet space flights are not fully understood. Mechanisms operative in regulation and maintenance of fluid and electrolyte balance during chronic exposure to microgravity are even less defined.

Regulation of body fluid and electrolyte balance is a fundamental homeostatic function. Severe dehydration or loss of electrolytes (especially sodium and potassium) can alter cardiac performance, skeletal muscle function, temperature regulation and cellular electrochemical gradients, potentially resulting in circulatory collapse. The regulation of fluid and electrolytes is essential to the ability to respond to physical and emotional stress. It is important to understand, as completely as

possible, the fluid and electrolyte changes that occur during exposure to microgravity, as well as changes in hormones and other factors regulating those balances. A more complete analysis of renal function, including changes in blood urea nitrogen and occurrence of kidney stones is required.

Research Requirements. Mechanical, dietary, behavioral, and chemical countermeasures will be evaluated for long-duration missions. Studies should include the magnitude, time course, and steady state levels of changes in key electrolytes within different body fluid compartments, throughout the process of adaptation to microgravity. The functional relationship between changes in fluid and electrolyte regulatory mechanisms and cardiovascular system deconditioning in microgravity should be studied. Ground models, such as antiorthostatic bedrest as a method of simulating microgravity for studying long-duration space flight induced alterations in fluid and electrolyte metabolism, and computer models, should be validated with humans in space. This is essential to enable screening of countermeasure systems for long-duration missions.

c. Hematology

Loss of red blood cell mass is a significant and consistent response to space flight. Further, it may represent a model of the effects of space flight on proliferative tissues. Despite substantial investigation in the United States and Soviet Union, the etiology, biological mechanisms, and potential operational significance of the loss of red blood cell mass have not been adequately defined. The loss undoubtedly contributes to orthostatic intolerance and decreased postflight exercise capacity. While the primary cause appears to be the influence of microgravity itself, the etiology is probably multifactorial, including influences such as hypokinesia and hypodynamia, bone demineralization and remodeling, muscle atrophy, altered hemodynamics, modified oxygen demand or oxygen carrying capacity, and nutritional and metabolic disturbances which in turn may be due to microgravity. The influence of other environmental factors such as hyperoxia, hypobaria, ionizing radiation, toxic contaminants, and accelerative stresses of space flight remains to be established.

Research Requirements. Available information does not permit extrapolation of the course of red blood cell dynamics during space missions lasting a year or longer. Nor can the possibility be ruled out that the loss of red blood cell mass could compromise the safety and effectiveness of crews in flights complicated by illness, injury, or life support equipment malfunction. Lack of information on mechanisms of red blood cell formation and release during space flight emphasizes the need to acquire more data. Moreover, uncertainties exist as to probable responses of the hematopoietic system during space missions lasting a year or longer. Therefore, reduction in red blood cell mass represents a contingent operational medical problem. Until the cause and mechanisms of these changes are understood, appropriate countermeasures cannot be developed and validated. However, infusion of red blood cells or erythropoietin are potential solutions.

d. Immunology

Pre- and postflight measurements have demonstrated that space flight causes a suppression of the cell mediated immune system, which returns to preflight levels within approximately 30 days after return to Earth. Due to limited inflight data, we do

not know: (1) inflight functional levels, or (2) the time course and magnitude of suppression. Therefore, we cannot predict whether functional levels could stabilize at a new depressed space flight homeostatic level or continue to decline. We cannot predict whether recovery will occur after extended duration missions. Furthermore, we do not know which space flight environmental factor causes the suppression, and we do not know the medical significance.

The immune system of higher animals protects the body from exogenous (e.g., infectious bacteria, fungi, and viruses) or endogenous (e.g., neoplastic) threats to survival. Surveillance and destruction of neoplastic or otherwise antigenically transformed cells before they can form a tumor and metastasize and spread cancer throughout the body will be particularly important in space because the relatively high radiation environment and potential for exposure to toxicants in closed cabins could increase the rate of mutation or tumorigenesis.

Research Requirements. The question of the time course, magnitude, and potential clinical significance of changes in immune competency must be addressed with a program of clinical and scientific investigations involving carefully designed and integrated ground-based and flight experiments. Space flight-related decrement(s) in immune function that would affect the identification and elimination of infectious organisms or surveillance of the internal environment for transformed cells must be identified. Their impact on crew health and safety must be assessed, and, if required, appropriate prophylactic or therapeutic measures developed. This is a particularly vulnerable area since state-of-the-art remedial procedures lag. It will be important to evaluate effects of space flight deconditioning and countermeasure procedures for beneficial as well as adverse effects on the immune system.

4. Neuroscience

Adaptation to space has a major impact on the motor system and on motor coordination because of the absence or reduction of gravity. Major neurological issues are shown in Table V-5. Antigravity muscles are unloaded continuously and antigravity reflexes, utilized in maintaining posture and locomotion on Earth, are inactive or modified. As a result, there is a loss of extensor reflexes in space. This may lead to the fetal posturing of legs that has been observed in space flight. Sensory information about limb position is not interpreted correctly in the absence of vision, and voluntary pointing accuracy and perception of static limb position are impaired. Upon return to Earth, there is postural imbalance and locomotor incoordination, including difficulty in walking and standing with eyes closed, and in executing quick turns. These symptoms occur even after relatively short missions where changes in muscle strength are minor. This indicates that such changes are largely due to lasting effects of adaptation of both central motor programs and the proprioceptive system. Anecdotal evidence from the Soviet space program of physical incoordination even several months after a mission, suggests that motor patterns may take a long time to readapt. The time required to fully readapt to preflight levels after very long periods of exposure to microgravity is unknown. A prolonged period of postural inactivation and impairment of locomotion would not be acceptable in the event of an emergency during the landing on Mars that demanded quick egress from the space vehicle. Moreover, it could also seriously impair the ability of astronauts to accomplish mission

tasks, or even care for themselves, in the Mars gravitational environment. There are no known countermeasures other than readaptation during exercise in a 1g environment.

**Table V-6
Neuroscience**

- • Determine sensory inputs and coordination of muscular function for generation of posture and locomotion before, during, and after flight
 - If an onboard centrifuge is used as a countermeasure, will repeated transition from 1-g to microgravity cause maladaptation
 - • Determine optimal countermeasures for motor readaption to partial gravity or 1-g after adaptation to microgravity
 - Determine whether the decrease in afferent input to the vestibular, proprioceptive, and somatosensory systems that are associated with long-duration space flight result in permanent reflex deficits
-
- = Required for Mars
 - • = Required for Moon and Mars

Research Requirements. Disabling motion sickness on return to a gravitational environment must be understood and alleviated. Studies of the motor system to understand and devise countermeasures to postural readaptation in space are required before a mission to Mars is possible. Important questions related to this objective include: (1) How are the sensory inputs and coordination of motor function organized for generation of posture and locomotion before, during, and after flight? (2) What adaptive processes modify motor control systems, including the oculomotor system? (3) What is the dynamic range of adaptation of motor responses in altered states of gravity? (4) What processes explain the altered perceptions of joint and body position in microgravity? (5) Will the decrease in afferent input to the vestibular, proprioceptive, and somato-sensory systems and the adaptation associated with long-duration flight result in permanent reflex deficits? (6) Are there morphological or structural changes in CNS and neuromuscular functions that form the basis for these deficits? and (7) If an onboard short-radius centrifuge is adopted as a physiological countermeasure, will humans be able to maintain a dual state of adaptation, and will they suffer from motion sickness when transitioning from microgravity to hypergravity?

5. Cell and Developmental

Cell and developmental studies provide the fundamental scientific knowledge and understanding of mechanisms necessary for development of effective countermeasures. Understanding the effect of the space environment on cellular and developmental processes (i.e., the generation, maintenance, differentiation, and turnover of tissue-specific cells) in adult humans is essential (Table V-6). These include erythropoietic stem cells (that produce red blood cells), osteogenic cells (that remodel bone), epithelial cells (that continually differentiate, function, and turnover) and the dynamic morphogenesis and differentiation of microvasculature. Cellular systems that have exhibited potentially serious alterations in space include: immune cell activation, muscle contractile activity and atrophy; mineralization-demineralization dynamics of bone and cartilage; secretory function of exocrine and endocrine epithelia; and cardiac myocyte electrical coordination. Changes in gene expression and altered mitotic activity (e.g., tumor formation) also fall into this category.

Table V-7
Cell and Developmental

- Determine microgravity adaptation and other space flight effects on musculoskeletal system responses including:
 - Biomechanical unloading
 - Fluid distribution, composition and pressure
 - Impacts on fluid homeostasis
 - Determine interactive effects of radiation and microgravity
 - How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?
- = Required for Mars
 •• = Required for Moon and Mars

Research Requirements. The key issues that need to be addressed are: What are the effects of reduced gravity or other space flight environmental factors on gene expression, cell division, cell differentiation, cell and tissue interactions, signal generation and reception, signal transduction and target response, endocytosis and secretory activity? It is essential that a variety of cell types (*in vivo* and *in vitro*) be analyzed for microgravitational effects to elucidate mechanisms and develop countermeasures that inhibit or reverse deleterious effects.

6. Artificial Gravity

It is highly probable that imposing some level and pattern of artificial gravitational force on humans over a period of months and years would be an effective countermeasure. However, there is little information available on the physiological effects of intermittent g loading or the effects of different levels of g loading. It would seem prudent to identify how variable levels of gravity can be used to normalize physiological processes. This program should identify the gravity levels that are necessary to maintain affected tissue and physiological systems, determine how these loads should be applied (e.g., continuous vs. intermittent), and provide protocols to minimize or eliminate undesirable side effects. Artificial gravity countermeasures should be integrated with other countermeasures such as exercise, hydration, and sensory-motor training. Additionally, these studies will contribute to our fundamental understanding of the effects of gravitational and coriolis forces on physiological systems. Artificial gravity may be necessary if other countermeasures are not sufficient for long-duration Mars missions. It is possible that artificial gravity countermeasures could reduce the cost and logistics burden while enhancing crew performance on Mars missions. The payoff for artificial gravity countermeasures or a continuous 1g environment on the transit vehicle will be larger if physiological adaptation to Mars gravity (0.38g) is significantly less than that experienced in microgravity, thereby allowing simpler countermeasures throughout the mission.

C. Constrained Program — Countermeasures for Crew Exposure to Space Flight Factors

Living systems have an exquisitely refined capability to integrate sensory input (e.g., visual, thermal, light, nutrient levels, gravity), coordinate global subsystem responses (e.g., circulatory, musculoskeletal), and produce a unified whole body response (e.g., redirect blood flow to body surfaces, sweat and increase water intake to adjust temperature). Furthermore, responses to inflight environmental factors could exacerbate the effects of microgravity (e.g., sleep disturbances and orthostatic intolerance). Therefore, it is artificial to separate the inflight effects of hypogravity from other space flight effects. However, the separation is pragmatically necessary, both for this plan and to design interpretable experiments. Countermeasure systems for these should be readily identifiable. The following life sciences disciplines address critical issues that primarily respond to space environmental factors (Table V-7), but include some aspects of hypogravity response:

- Behavior and Performance
- Environmental Health
- Regulatory Physiology.

Table V-8
Spacecraft Cabin Environmental Factors

Pressure
Temperature
Gas composition
Microbiology and Toxicology (quality/quantity)
Lighting (intensity, quality, duration)
Food (quality, diversity, quantity)
Restricted habitability and personnel hygiene standards
Confinement and isolation
Potentially sustained stressful situations

1. Behavior, Performance and Human Factors

Most of the research in this area is required for a Mars mission, of even the shortest possible duration. The overall issue is effective functioning of a crew enclosed in a confined environment in microgravity and subjected to continuous operational and environmental stress (Table V-8). Problems of morale, hostility, and breakdowns of communication have been documented with increasing frequency as the duration of the interaction increased, even in ground-based operations. Problems are compounded by the stresses of space, for example: (1) deconditioning in microgravity; (2) closed environmental life support systems; (3) unpredictable risk of radiation exposure beyond the magnetosphere; and (4) limited (low Earth orbit and Moon) or extremely long- duration (Mars) escape or abort capability.

Although data are limited, both the U.S. and Soviet space programs have documented behavioral problems, including fatigue, irritability, depression, anxiety, mood fluctuations, boredom, tension, social withdrawal, and motivational changes. Instances of hostility between flight crewmembers, and space and ground crews have been reported. Data from short-duration (10-day) space flights demonstrate

Table V-9
Behavior, Performance, and Human Factors

- Determine criteria for evaluating individual and crew performance/productivity
 - Determine effects of prolonged space flight on behavior and group dynamics (including differences such as age, sex, culture)
 - Determine critical characteristics of leader influence on productivity and stability among crewmembers
 - Define optimal crew command structure for Moon and Mars missions
 - Establish protocols for training effective ground and space crews in such areas as enhanced communication, crew coordination, interpersonal dynamics, and problem solving
 - Determine requirements for optimal integration of automated systems with human capability to maximize productivity and reliability.
-
- = Required for Mars
 - = Required for Moon and Mars

Although data are limited, both the U.S. and Soviet space programs have documented behavioral problems, including fatigue, irritability, depression, anxiety, mood fluctuations, boredom, tension, social withdrawal, and motivational changes. Instances of hostility between flight crewmembers, and space and ground crews have been reported. Data from short-duration (10-day) space flights demonstrate deleterious effects on physical performance, particularly disturbances in sensory-motor systems, visual function (e.g., illusions) and proprioception. Some reflexes are slightly impaired early in flight but recover after adaptation. Postflight data show similar visual function impairments, including illusions and mass discrimination deficiencies. Explanations of these phenomena include changes due to learning of new perceptual and motor skills and/or effects of spatial disorientation and space motion sickness. The evidence from short-duration space missions indicates that behavioral capabilities can be maintained during space flight despite small decreases in work capacity early in flight. There is no database for long-duration missions.

Investigations of sleep patterns and performance have been conducted on several short-duration missions. Poor sleep quality and fatigue have been reported and approximately 30% of U.S. Shuttle astronauts have requested sleep medication in flight, though none had a history of usage on Earth.

The psychosocial dynamics of small groups of humans living in confined and isolated environments for prolonged periods are not well understood, even for ground operations. Critical issues focus on interactive crew behavior and performance. Selection criteria for crew composition and structure, and training protocols are key areas. They must consider the individual in the context of the group including suitability of skill mix and interpersonal attributes. Selection criteria that address leadership, and its impact on order, morale and group cohesion are critical.

Research Requirements. The most critical research elements include: how the individual will perform; how the group will continue to function effectively; monitoring and compensation strategies for environmental stresses; optimal integration of automation and human capabilities; and crew selection criteria. Behavior and performance countermeasures include: performance evaluation criteria; monitoring

and control strategies for performance-related stress effects; mission stage-specific assessments of physical and cognitive performance capabilities; crew selection criteria related to group productivity and stability; protocols for enhanced communications; and development of special EVA performance requirements. Research elements related to performance and group functioning include: microgravity and other space environment factors effects on fundamental behavioral processes such as perception, sensation, learning, and motor skills; physiological changes and reliable correlates of performance; circadian rhythms, sleep patterns and work/rest schedules; and individual and team motivation and coping strategies for environmental stressors. Supporting research includes workloads, schedules, interactions with ground support teams, nonintrusive performance data collection, and modeling of complex performance.

A carefully integrated sequence of events, programmed to facilitate crew selection, should remain sufficiently resilient and elastic to incorporate modifications as the state-of-the-science advances. The process should include: (1) psychological testing to "select out" and "select in" candidates on the basis of personal and group interviews and psychological tests followed by group situations to determine compatibility; (2) simulation training of candidate crews in a high fidelity Mars transfer vehicle mock-up (a confinement period of three to four months will be required to gain experience and data on crew compatibility and performance); and (3) SSF testing for a three to four month exposure to test crew compatibility and performance in microgravity and to provide information for designing the Mars transit vehicle and base.

2. Environmental Health

The major environmental health issue for countermeasures involves adaptative responses of the body to altered pressure, varying concentrations of gases and contaminants (Table V-9). Problems associated with reduced pressure include decompression sickness and physiological problems associated with environmental gas concentrations, including hyperoxia and hypercapnia. Physiological monitoring equipment is required to study the effects of alterations in the environment on cardiovascular, regulatory, neurosensory, musculoskeletal, behavioral (performance), and other systems. Countermeasure systems will include surveillance, detection, warning, and remediation.

Table V-10
Environmental Health

- Determine effects of prolonged exposure to microgravity and other space flight environmental factors

•• = Required for Moon and Mars

Research Requirements. Ground-based research should include studies on decompression sickness, mechanisms leading to countermeasures that facilitate safe EVA, optimal suit pressures, and gas compositions. Ground-based research and flight investigations should address the interaction of hyperoxia, hypercapnia, hypoxia, hypobaria, decompression sickness, ambient pressure, and microgravity. Ground-based research also includes the development of protocols for training to cope with

decompression sickness and other adverse physiological responses. Research to develop models to predict physiological response to varying environmental conditions is also needed.

3. Regulatory Physiology

a. Circadian Rhythms/Sleep

Circadian rhythms (i.e., characteristics of living systems that cycle with a relatively fixed and predictable period of about 24 hours) are a fundamental property of most organisms. Circadian rhythmic variations are observed in almost all biochemical, cellular, physiological, and behavioral systems. These rhythms are generated by internal (i.e., endogenous) biological clocks that are normally entrained or synchronized to 24-hour changes in the physical environment by external signals (e.g., light-dark cycle). Extensive biochemical, molecular and cellular studies are ongoing to elucidate the biological mechanisms by which circadian rhythms are generated and entrained.

Biological rhythms are a common feature of regulatory systems, and the proper timing of circadian rhythms is vital for optimal health of organisms. Recent studies of humans focus on the importance of circadian rhythms and sleep for normal mental and physical health, and on methods to influence them for optimizing performance in a variety of work environments. Understanding and managing circadian rhythms in the absence of the normal 24-hour cycle of Earth signals is critical for crew health and performance.

Research Requirements. Countermeasures would include the design of lighting systems, imposed work/rest schedules, time-of-day scheduling of activities such as EVA and exercise, and use of pharmacological agents.

b. Metabolism/Nutrition

Metabolic status and nutritional requirements of humans are affected by changes in physiological state. Responses to weightlessness, limited food choices, and exposure to radiation during space flight could affect human metabolism and nutritional requirements, which in turn affect physiological systems. Thus, metabolic regulation and nutritional balance are integral parts of maintaining health and performance in space. In addition, long-duration effects of space flight on gastrointestinal (including liver) and kidney function and absorption of nutrients are unknown.

The therapeutic effect of drugs depends on the rate at which they are absorbed, metabolized, and eliminated; and on their distribution within the body. Changes in gastrointestinal, hepatic, or renal function or in circulatory dynamics may modify drug pharmacodynamics.

Long-term exposure to microgravity may change metabolic and energy requirements. Therefore, metabolic efficiency and steady state energy expenditure in space during nominal activities, exercise, and EVA should be determined. If there are changes, physiological factors must be elucidated and countermeasures must be developed.

Research Requirements. Countermeasures, discussed in other parts of this report, are being considered for bone demineralization, cardiopulmonary function, muscle atrophy, fluid shifts, electrolyte imbalances, etc. All of these are affected by metabolic and nutritional status. Therefore, nutritional countermeasures are an integral component of other countermeasure systems. For example, exercise is a primary countermeasure against muscle atrophy, and may be useful in minimizing bone demineralization, and provision of special amino acid combinations could aid in preventing muscle atrophy.

c. Temperature Regulation

Temperature regulation is an example of a highly complex, integrated regulatory system that maintains homeostasis in the face of wide variations in environmental conditions. In humans, except for an occasional episode of fever or exercise-induced hyperthermia, body temperature rarely varies more than two degrees centigrade from baseline throughout an individual's lifetime. A normally functioning thermoregulatory system is vital for the health of the individual. For example, thermoregulation is drastically impaired by body fluid alterations during dehydration. Sustained high fever can cause severe damage and even death. Even transient exposure to high or low temperature leads to discomfort and radically impairs sleep and performance.

Alteration of core body temperature observed on COSMOS and Spacelab flights led to numerous thermoregulation studies which document the effect of space flight. Anecdotal data from U.S. and Soviet space studies suggest that there may also be a shift in the thermal comfort zone. Current evidence suggests changes in the capability to homeostatically respond to altered thermal environments (i.e., ambient temperature) or loads (i.e., exercise or EVA). Other components of the space flight environment (e.g., light, pressure, and gas composition) may also alter this system.

Determination of whether a countermeasure system is necessary and establishment of design requirements await further understanding of the effects of space flight on thermoregulation. However, cooling garments have already been used for EVA, and environmental health and hydration strategies may provide simple countermeasures for extended duration missions.

D. Robust Program

The robust program for CS would include development of artificial gravity countermeasures capability as a parallel program with other microgravity countermeasures. The engineering requirements to deliver artificial gravity (e.g., tethers, rotating space craft, short-armed or long-radius centrifuges) would be developed in conjunction with EHLSS applications.

Artificial gravity is the only alternative for a Mars mission, if countermeasures currently being investigated in low Earth orbit are not sufficient for long duration missions. An artificial gravity countermeasure program would begin with investigation of the effects of intermittent g at various g-loads, rotation rates, and frequencies with and without activity as a universal or partial CS. It would include intensive, highly focused studies on the effects of 0.16g and 0.38g. Some studies of intermittent g and the effects of continuously rotating environments can be conducted on the ground using simulators

and models. Most of this research will require small variable g centrifuges for a variety of diminutive model organisms and the Centrifuge Facility on SSF. Facilities on the Moon will enhance this research.

Slow rotating rooms will be used to examine the chronic physiological effects of continuous rotation on humans in 1g. The robust program would include a human variable gravity research facility in space to support basic investigations of the efficacy of fractional gravity in attenuating the effects of prolonged exposure to microgravity conditions. This facility would investigate human performance in a prolonged microgravity condition, habitability-related problems of working and living in a partial or intermittent gravity environment, effects of variable-rotation rate, level of artificial gravity required, and effect of duration, performance and productivity. It would evolve to become a full scale prototype used to simulate different scenarios and phases of Moon and Mars exploration missions.

A robust program will include advanced computer models and simulators for all components of the constrained countermeasures program. It will accelerate inclusion of artificial intelligence capabilities and will include enhancements in the basic science studies focusing on the mechanisms which underpin countermeasures development.

The robust program will investigate the extensive knowledge base resulting from experiments on estivation and hibernation in animals both to: 1) understand how modifications in body systems compensate for inactivity, which may provide totally new insights for countermeasures, and (2) to understand how changes in the environment and internal control systems initiate and control reduced metabolic activity, which may provide an initial pathway toward the benefits which would derive from a suspended animation-like capability for long-duration space missions.

E. Requirements for Moon Exploration Missions

Because of the relatively short Moon recovery time and mission duration, Countermeasure Systems can evolutionarily build in complexity from SSF capabilities until they incorporate a full scale operational test of Mars mission capabilities. The boxed lists in the previous discussion identify issues that are not required for Moon missions. The identified differences in life sciences research and technology programs for Moon and Mars missions are due to differences in mission durations and rescue times. Development of countermeasures for Mars missions will require extensive data on long-term effects of hypogravity and other space flight environmental factors, and better understanding of the underlying mechanisms in the musculoskeletal, cardiovascular, regulatory physiology, neuroscience, cell and developmental, and behavior, performance and human factors areas.

VI. MEDICAL CARE SYSTEMS

A. Introduction

An appropriate level of inflight medical care is a critical element in overall mission success. The capability to treat a broad range of medical and surgical conditions is justifiable both for humanitarian reasons and to ensure that the crew is healthy enough to perform their assigned duties. As a general principle, increasing isolation and mission hazard should be countered by an increasingly capable and autonomous health care system, although it is axiomatic to note that not all clinical conditions will be treatable in space. The overarching objective is to provide treatment capabilities for most feasible conditions without imposing an unacceptable burden on the constrained resources available within spacecraft and planetary habitats. Thus, the overarching MCS requirement is research and development needed to determine potential risks and to identify the mission resources required. Studies must include trade-offs between onboard medical capability and rescue capability (e.g., Assured Crew Return Vehicle for SSF).

Countermeasures and medical care systems form a continuum in terms of overall crew health. Countermeasures represent a preventive medicine approach to limit the deleterious medical effects of unopposed space flight deconditioning, where the medical care systems provide clinical treatment for overt illness or injury. Medical care system requirements result from endogenous medical risk (i.e., that which any individual has as a result of hereditary, lifestyle, and prior illness), unopposed physiological deconditioning in microgravity, environmental factors (radiation exposure, atmospheric contamination, or rapid pressure changes) and psychological stress associated with living and working in an isolated, hazardous and confined environment. The body's tremendous ability to acclimate, both: (1) allows humans to exist in a microgravity environment which was not experienced during the evolutionary process; and (2) confounds medical treatment in space. Many physiological parameters change in the flight environment. It is not known whether the degree to which these changes occur are simply appropriate adjustments to a new "normal" homeostatic level suitable to that environment. Consequently, it is not known when or if intervention to adjust parameters toward "Earth normal" is beneficial; and diagnosis and treatment of illness without a clear definition of "normal" is difficult at best.

Exposure to the space environment is known to cause changes in drug kinetics, absorption, and action, increases in size of internal organs (e.g., the spleen), changes in the shape and function of the heart and vessels, and multiple alterations in regulatory physiology. The clinical significance of these alterations is not yet clear due to limited experience with medical observation and care inflight. Furthermore, the broad issue of clinical response of the space-adapted crewmember to pathological conditions (e.g., hemorrhage, fracture or lacerations) has not been addressed. It is possible that modified disease processes will require a different approach for providing medical care.

Table VI-1 identifies the Life Sciences Division disciplines¹ that support solutions in clinical medicine and therapeutic response, and summarizes other requirements for MCS.

TABLE VI-1			
PROVISIONS FOR MEDICAL CARE SYSTEMS			
ILLNESS AND INJURY EVENTS	SYSTEMS PROVIDING CAPABILITY		
	ENVIRONMENTAL HEALTH & LIFE SUPPORT	COUNTER-MEASURES**	MEDICAL CARE
Occupational Health:			
Endogenous medical risk factors			X
EHLSS failure or degradation			C
CS failure or inadequacy			C
Surgical and medical regimes:			
Cardiopulmonary		X	C
Musculoskeletal		X	C
Metabolic Disorders**		X	C
Radiation Health		X*	C
Cell and Developmental Function		X	C
X — Implies the potential for a solution C — Contingency capability for limited and temporary intervention or treatment * — If synergism between microgravity and radiation exists ** — Pathological regulatory physiology			

B. Constrained Program — Surgical and Medical Regimes

1. Cardiopulmonary System

Medical care systems for exploration missions will require the ability to diagnose and treat major cardiopulmonary emergencies, including but not limited to:

- Decompression sickness (not exclusively a cardiopulmonary problem)
- Myocardial infarction (heart attack)
- Pulmonary embolus
- Cardiac arrhythmias/angina/congestive heart failure
- Cardiopulmonary arrest.

Footnote 1. Less than one percent of the critical questions in Life Sciences Division Discipline Science Plans support a constrained program in Medical Care Systems. See Volume II, Table 2 for details.

Table VI-2
Cardiopulmonary

- Determine beneficial and harmful delayed or persistent consequences of long-term space flight and identify appropriate short-term (i.e., hours to days) and long-term (i.e., months to years) postflight rehabilitative measures
 - Identify risks for bubble formation and decompression sickness associated with pre-EVA denitrogenation/decompression schedules and exercises
 - Determine cardiovascular electrical and mechanical responses to EVA at different levels of gravity (e.g., transit and surfaces of Moon and Mars)
--Determine what factors influence the occurrence, magnitude, and sequence of these responses
 - Establish pulmonary life support procedures for protection or resuscitation in the event of loss of EVA suit or cabin pressure, and for cardiopulmonary resuscitation and general anesthesia
 - Determine whether space flight increases cardiac arrhythmias and identify mechanisms
 - Determine whether the extent of adaptation to space flight affects postflight orthostatic intolerance
 - Determine space flight alterations in blood pressure and flows and functional consequences in tissues and organ systems during long-duration flight or after return to Earth
- = Required for Mars
 - = Required for Moon and Mars

Research Requirements. Additional study of decompression sickness (bends) and design of improved space suits is required. Ground EVA simulations suggest that bubbles frequently occur in the pulmonary artery, but that clinical bends occurs much less frequently. While bubbles may be of little consequence in a normal subject, they could be catastrophic in a subject with an undetected arteriovenous shunt. Risks of bubble formation and clinical decompression sickness associated with pre-EVA denitrogenation/decompression schedules and exercises must be identified. Standards for crew health and performance, including periodic monitoring of health status, must be developed. The impact of expanded EVA (e.g., constructing SSF) and EHA (base construction and Moon or Mars exploration) on the risk of decompression sickness and suit design must be determined.

Certain types of arrhythmia will incapacitate a crewmember and endanger a mission. Therefore, it is important to know whether the prevalence of cardiac arrhythmias is in fact higher during space flight, and if so, what mechanisms, prevention, and therapy are required. It is important to determine whether space alters pharmacokinetics and dose response curves for beneficial and deleterious effects of anti-arrhythmic and other cardioactive and vasoactive drugs. An understanding of the mechanisms and treatment of orthostatic intolerance that could compromise landing and productivity on the Moon or Mars, and on return to Earth is required. What is the threshold for prevention of intolerance (e.g., will 0.16 or 0.38 Earth gravity prevent its occurrence?), and are there more effective and/or less intrusive methods of therapy than those currently employed (e.g., fluid loading, lower body negative pressure—LBNP)?

2. Musculoskeletal

Major issues (Table VI-3) involve the prevention of excessive deconditioning and the provisions for treatment of acute injuries. There is substantial risk of a crush injury of muscle and bone when moving large masses in space; and muscle and tendon sprains, bruises, and bone fracture with work or exercise. Prevention of excessive deconditioning is necessary because:

- 1) Excessively deconditioned crewmembers may not be able to respond to inflight or postflight situations requiring physical strength and stamina.
- 2) Routine EVA activities, which will characterize planetary surface exploration programs, will require normal physical strength and stamina.
- 3) Crewmembers with excessive deconditioning will be prone to bone fractures, tendon injuries, or muscle tears while doing physical work and/or exercising.

**Table VI-3
Musculoskeletal**

- Define the risk for bone loss on development of bone fractures, hypercalcemia, metastatic calcifications, and renal stone formation
- Determine whether atrophy from unloading makes muscle, tendon and the myotendinous functions more susceptible to injury or damage on resuming normal weight-bearing status
- Determine how well injured muscles repair in microgravity
- = Required for Mars

While prevention will be the primary MCS thrust, diagnosis and treatment must be available for fractures, repair of ruptured tendons and ligaments, and prevention or treatment for complications of fractures (e.g., pulmonary embolus). Diagnosis and treatment must be provided for the secondary effects of muscle and bone tissue wasting which may lead to mineral and electrolyte derangements. These include hypercalcemia (which could cause metastatic calcification), muscle weakness, changes in mental status, hypercalciuria (which leads to kidney stones and dehydration), and hyperkalemia (which could cause cardiac arrhythmia).

Research Requirements. Studies are needed to elucidate the biomechanics of work/exercise in microgravity and partial gravity, both for activity within the vehicle and EVA environments. The nature and mechanism of bone, skin, and muscle healing in microgravity must be determined.

3. Metabolic Disorders (Pathological Regulatory Physiology)

The critical research elements for exploration missions include the effects of microgravity on renal function, endocrine changes that effect the functioning of other homeostatic systems, drug effectiveness, and the combined effects of microgravity and EVA on thermoregulation and heat exchange (Table VI-4). The specific effects of the demonstrated immunological and metabolic alterations of microgravity on the host defense response to severe infection should be investigated. The role of countermeasures in the control of septic processes in microgravity also must be defined and their interactions quantified. Critical care, diagnosis, and treatment should be available for renal failure and common clinical endocrine problems.

**Table VI-4
Regulatory Physiology**

- Determine effects of space-induced endocrine changes on the function of other homeostatic systems (e.g., cardiovascular, CNS, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism, sleep, behavior and performance
 - Determine effects of microgravity on renal function. Are effects progressive or reversible? Are there differences in filtration, reabsorption, secretion, and excretion?
 - Determine the nature of space flight induced effects of vasoactive, pharmacokinetic and other drugs
 - Determine effects of space flight and EVA on thermoregulation and heat exchange
-
- = Required for Mars
 - = Required for Moon and Mars

Research Requirements. A key challenge within the area of regulatory physiology involves the identification of "normal" parameters for the space-adapted individual. These clinical norms are essential to the practice of medicine in the space environment because clinical decisions are often made on the basis of deviations from a baseline value. Both animal and human studies have shown marked variations of endocrine function, examples of which include a tendency towards glucose intolerance (diabetes) and marked decreases of certain regulatory hormones (such as testosterone) in flight. The medical and operational impacts of these changes must be assessed.

4. Radiation Health

The radiation environment for space exploration is not yet sufficiently understood, but on the basis of what is known about exposure to ionizing radiation, it is likely to have serious health implications. The primary research elements for radiation health were presented in Section I (EHLSS). The important research elements from an MCS perspective are discussed below.

Solar particle events (SPEs), commonly referred to as solar flares, pose a life threatening radiation health risk for crewmembers outside the spacecraft and on planetary surfaces. Therefore, the provision of a sanctuary to limit radiation dose is a medical requirement. Determining the degree to which radiation impacts on bone marrow and lymphoid tissue responses will impair the containment of invasive sepsis, thereby preventing generalized septic response, is an important medical question.

**Table VI-5
Radiation Health**

- Develop protocols to manage medical risks associated with acute and chronic exposure to space radiation
-
- = Required for Moon and Mars

Determining the long-term medical consequences of exposure to high Z element (HZE) particles present as a component of galactic cosmic radiation (GCR) is critical. The biological hazards associated with HZE particles, i.e, the "late effects," are not adequately known and may pose unacceptable long-term cancer risks. Exposure can result in life-threatening and life-shortening effects, such as cancer, and other detrimental consequences including cataract formation, mutagenesis, and other tissue damage. Neurological and behavioral effects and their consequences on crew performance must also be understood.

Research Requirements. In order to accomplish a realistic risk assessment for radiation exposure during exploration missions, the fluency of GCR, and its biological effects, must be determined prior to establishing medical standards for radiation exposure in space. Other related issues include crew selection standards, personal radiation protection, and medical protocols for treatment of radiation sickness.

5. Environmental Health

The critical issues focus on the treatment of medical problems related to adverse temperature and gaseous environment conditions, procedures to prevent and minimize the risk of decompression sickness, and assessment of EVA risks (Table VI-6). Also included are microgravity effects on the immune system and the degradation or failure of the life support system.

**Table VI-6
Environmental Health**

- Determine treatment of medical problems related to spacecraft inner temperature and adverse effects of the gaseous environment
 - Determine procedures and approaches to prevent decompression sickness or minimize crew risks
 - Determine risks and risk relationships among detectable gas emboli, mild limb bend symptoms that impair performance, and both CNS and cardiovascular systems that are life threatening under EVA conditions
 - Determine effects of long-duration space flight on the human immune system
-
- = Required for Mars
 - = Required for Moon and Mars

Research Requirements. There are several medical concerns related to environmental health which generate research requirements. A key concern relates to the medical consequences of continuous exposure to low level atmospheric contaminants. An obvious difference between Earth-based occupations and extended space missions is that individuals essentially live in the workplace, without the exposure relief that a terrestrial worker gets when leaving the job. Applicable exposure standards, treatment protocols and risk assessment protocols which take into account the changes in the immunological system will have to be developed. The physiological effects of long-term exposure to hypobaric, normoxic environments (should a reduced pressure spacecraft be selected) is an area of great uncertainty in aerospace medicine. The longest hypobaric U.S. mission to date was the 84-day

Skylab 4 mission. A related concern is the medical effects of extended habitation in a spacecraft with a degraded life support system.

6. Cell and Developmental Function

Critical issues in this area focus on providing the scientific knowledge necessary for development of procedures for risk management of pregnancy, osteoporosis, and hemorrhage; determination of whether microgravity effects can be reversed; characterization of the influence of radiation and microgravity effects on development of germ cells; and determination of the effects of gravity on compensatory endocrine, organ, circulatory, regenerative mechanisms, interaction with growth stages, and wound healing (Table VI-7).

Table VI-7
Cell and Development

- Establish management procedures for premenopausal female crewmembers to minimize risk of pregnancy, osteoporosis, and hemorrhage
 - What is the role of gravity in developmental biology?
 - Determine effects of gravity on compensatory mechanisms (e.g., (endocrine, organ, circulatory, regenerative), interaction with growth stages, and wound healing
 - Determine whether gravity-related effects exist and if they can be reversed
 - What is the result of gravity-induced desynchronization during development?
-
- = Required for Mars
 - = Required for Moon and Mars

Estrogen enhances retention of bone minerals and reduces development of heart disease. It is therefore essential to maintain normal estrogen levels in female crewmembers. However, except in postmenopausal females, normal estrogen production is coupled to ovarian cycles and ovulation and thus there is the possibility of ruptured follicles or pregnancy. Both of these conditions entail significant risk and could become life-threatening in space, but could be prevented by oral birth control methods. However, experience on Earth indicates that those methods are not completely reliable. Recently available progesterone-derivative implants (i.e., "Norplant"), or gonadotrophic release hormone agonists coupled with low-dose triphasic steroid replacement, might be improvements. However, these hormone protocols may have changing dose requirements over time in the space environment, and therefore would require monitoring to allow for periodic adjustment of doses. Also, interactions between estrogen levels and microgravity effects may be synergistic in bone.

Research Requirements. Studies done in Soviet biosatellites suggest that embryogenesis is disrupted or altered by microgravity. This concern and the obvious problems of dealing with childbirth and childcare in the space environment make pregnancy contraindicated during space missions. Research concerns, therefore, are focused on the potential medical consequences of contraception in microgravity, i.e., formation of blood clots, osteoporosis, and behavioral effects. Another high level research concern relates to the function of individual cells in microgravity. Most studies have focused upon physiological systems, rather than cellular function. This is

an important concern across a broad range of issues, including immune function; wound healing in various tissues (examples being corneal abrasions, skin lacerations, or bone fractures); drug transport across cellular membranes, inflammatory and allergic reactions; blood coagulation (vis a vis the role of cellular elements); and repair of damage from radiation. This is not a comprehensive list, but is a sample of potential concerns. In many cases, the demonstration of competence of cellular function in a given area (such as wound healing) will meet the research requirements. In other areas, such as osteogenesis, it may be necessary to understand the mechanics of cellular function in order to design effective countermeasures.

C. Advanced Medical Care Systems

U.S. and Soviet space programs have shown that medical contingencies do occur in flight. Most U.S. space flight medical care experience has been limited to minor ailments such as abrasions, contusions, colds, and space motion sickness. The medical care systems aboard Mercury, Gemini, and Apollo were essentially enhanced first aid kits equipped with bandages, ointments, drugs to treat a limited set of medical conditions, and instruments for medical exams. Skylab, an early second generation MCS, included provisions for minor surgery and dental procedures. The medical care facility planned for SSF, the Crew Health Care System (CHeCS), contains three subsystems: clinical care; exercise countermeasures; and environmental monitoring. Mature requirements for surgical facilities in space have not yet been established. This system is an advanced second generation of inflight medical care and requires significant technology development in the following areas (not an all-inclusive listing):

- Compact digital radiography
- Compact clinical chemistry analyzers
- Environmental monitoring technology (based on mass spectrometry)
- Medical data collection, storage, and transmission.

Exploration missions will require an unprecedented level of inflight medical care capability. Because of the extended duration, extreme distance from medical care facilities, hazards associated with operational tasks (EVA, EHA), and the delayed communications because of interplanetary distances. These systems will evolve from and build upon the clinical care systems used on SSF. These "third generation" medical systems will require significant technology development in key areas such as:

- Compact bone density imaging system
- Advanced telemedicine and telemetry capability for medical imaging (x-rays, scans), medical data, and text
- Computer-aided medical diagnostic, monitoring, and therapeutic systems
- Compact soft tissue imaging systems (presumably derivations of existing ultrasound imaging)
- Capacity to conduct major surgical procedures.

Advanced Biotechnology Development. While key elements of advanced hardware can be derived from existing terrestrial medical devices, some applications are unique to extended space flight and will require technology development efforts. For example:

- Extended shelf life (up to three years) pharmaceuticals
- Extended shelf life blood substitutes or blood (e.g., a lyophilized product)
- Research and development of liquid/gas separation devices. (Suction capability is needed for medical, surgical, and dental procedures)
- The ability to bank lymphocytes or derive biological products (lymphokineses). An advanced cell culture device (i.e., bioreactor) will be required. These cells will be required to bolster immune function in space, particularly after infection or radiation exposure
- Development of implanted ion selective electrodes and other sensors that allow continuous monitoring of key physiological parameters.

D. Robust Program

In addition to the constrained program as outlined, a robust program would include the following elements. These elements would limit the risk associated with long duration exploration missions to a greater degree than would the constrained program.

- Renal dialysis
- Skin grafting
- Enhanced major surgical capability (would include more invasive and complex procedures such as pinning bones). The exact menu of procedures included in constrained or robust programs would be determined in a trade study
- Advanced imaging and diagnostic capabilities, such as magnetic resonance imaging (MRI) or computerized tomography (CT) scans would be possible elements of a robust program. This also would be determined by trade studies
- Crew medical personnel would be different across the two programs. While even the constrained program would contain a physician (probably a surgeon), the robust program may be characterized by a second health care specialist, such as a psychologist or psychiatrist
- A robust program would be characterized by the ability to maintain crewmembers as inpatients for longer periods of time (up to six months) and would include the capability for extended parenteral (venous) feedings.

E. Requirements for Moon Exploration Missions

The medical care program for Moon missions would be similar to extended deep space missions, with the exception that provisions for certain types of injuries, more likely in the Moon environment, would be baselined. These might include treatment for crush injuries, electrical burns, or other types of occupational injuries that are more likely given the broad range of planetary surface activities planned for a Moon outpost. The exact set of capabilities would be determined by a detailed trade study and should be matched to the scope of surface activities. Because of the relatively short Moon recovery time (< 4 days), Moon medical care facilities, equipment, procedures, and protocols can build in an evolutionary fashion from SSF capabilities until they incorporate a full scale operational test of Mars mission capabilities.

SECTION VII

APPENDICES

- A - Description of Process
- B - Aerospace Medicine Advisory Committee (AMAC)
Membership List
- C - AMAC Charter for this Report
- D - Executive Steering Committee Membership List
- E - Life Sciences Advisory Subcommittee (LSAS)
Membership List
- F - Discipline Working Groups Membership List
- G - Bibliography
- H - Requirements for Ground-Based and Flight
Programs
- I - Acronym Listing

APPENDIX A DESCRIPTION OF PROCESS

DISCIPLINE WORKING GROUPS¹

Over the past two years, the Discipline Working Groups developed Discipline Science Plans for each NASA Life Sciences Division science disciplines. The plans describe the research required to support NASA life sciences goals and responsibilities.

NASA Life Sciences Goals	
Goal —	Ensuring the health, safety, and productivity of humans in space
Goal —	Acquiring fundamental scientific knowledge in space life sciences

The discipline plans, which include lists of critical questions that are prioritized within subdisciplinary categories, are:

1. Behavior, Performance and Human Factors
2. Regulatory Physiology
3. Cardiopulmonary
4. Environmental Health
5. Musculoskeletal
6. Neuroscience
7. Radiation Health
8. Cell and Developmental Biology
9. Plant Biology
10. Life Support, including CELSS
11. Planetary Protection
12. Exobiology

EXECUTIVE STEERING COMMITTEE²

GOALS

1. Define a robust research program and identify priorities required for exploration class missions based on current knowledge and the projected and realistic resources within the next 5 to 15 years. Include ground-based research, availability of facilities, flight opportunities, and international cooperation. Identify the risks associated with the proposed program.
2. In the event that a robust program is not possible, due to constraints such as availability of projected resources or schedule limitations, is there an alternative option for an adequate program? Identify the risks associated with such a program.
3. What are the most important (from a life sciences standpoint) robotic precursor missions and planetary protection research to be undertaken prior to human exploration?

Footnote 1. Discipline Working Groups — Extramural and center advisory groups (membership in Appendix F) that in conjunction with the Life Sciences Division Discipline Scientists, developed Science Plans (including a total of 500 critical questions) for each of the 12 NASA Life Sciences, science disciplines: Behavior, Performance and Human Factors; Regulatory Physiology; Cardiopulmonary; Environmental Health; Musculoskeletal; Neuroscience; Radiation Health; Cell and Developmental Biology; Plant Biology; Life Support, including CELSS; Planetary Protection; Exobiology.

Footnote 2. Executive Steering Committee — Discipline Working Group Chairpersons (see Footnote 1) or alternates, plus Headquarters and Center program managers and scientists (including program office representatives from Space Shuttle, Space Station Freedom, Aeronautics Exploration and Technology) who evaluated, revised and prioritized critical questions from Life Sciences Discipline Science Plans and developed a summary White Paper. See Appendix D for details of membership.

APPENDIX A DESCRIPTION OF PROCESS

4. Unrelated to applications, define the most promising and unique science activities that would be enabled by exploration mission(s).

STEP 1 *Identify What Needs To Be Known.*

Discipline Plans. The science discipline plans constitute the unconstrained Space Life Sciences program. The critical questions contained in the plans form the basis for determining recommendations.

For each discipline, identify and categorize all critical questions within each subdiscipline according to the following five categories: Each question may apply to more than one category. However, indicate the primary category of application by noting so with an asterisk ("**"). The committee was partitioned into discipline groups for completion of step 1 through step 5.

Categories for Research Program Critical Questions:

1. **Environmental Health and Life Support Systems:** Focuses on the activities required for sustaining a safe, livable, and habitable environment (artificial gravity can be considered during deliberations).
2. **Countermeasure Systems:** Assumes microgravity transfer vehicle. This includes activities required for developing, testing and validating countermeasures to ensure crew health and performance, and to minimize health risks throughout the mission(s).
3. **Medical Care Systems:** Focuses on activities required for acquiring the knowledge, procedures, and technology necessary for ensuring crew health.
4. **Enabled Science:** Activities that include the most promising and unique science enabled by exploration mission(s).
5. **Basic Science:** Activities that are not necessarily related to exploration missions, but offer scientifically promising and unique opportunities to pursue fundamental knowledge.

STEP 2: *Assumption for Assessing Criticality*

If the Agency commits to going to Mars (i.e., a 2014 - 2018 time frame) with a crew of five or six, identify within your discipline the critical questions for such a mission. Assess the criticality of each according to the scale below, and record your response in the appropriate column on the data sheet.

Criticality Scale

Level 1	Consensus That Answer Is Required For Mars Missions (Known Effect And Known Problem For Mission)
Level 2	Answers Might Be Required, But The Science Basis To Evaluate Risk Is Not Adequate
Level 3	Required For Practical Optimization of Resources (Or Counter measure Effectiveness) And Minimalization Of Risk
Level 4	Important Science That Is Relevant To Exploration Mission(s).

APPENDIX A

DESCRIPTION OF PROCESS

STEP 3: *Assess Science Readiness Status for Research and Missions (For each critical question identified in Step 2)*

Science Readiness Levels

Level 1	Only Folklore of Practitioners And Anecdotal Data Available
Level 2	Basic Scientific Concept Formulated
Level 3	Ground Models Developed, Flight Validation Required
Level 4	Flight Validation Performed
Level 5	Countermeasures Identified
Level 6	Countermeasures Tested
Level 7	Operational Requirements Established

STEP 4: *Assess the Readiness of Technology Necessary for Research or Missions (For each critical question identified in Step 2)*

Technology Readiness Levels

Level 1	Technology Need Identified
Level 2	Technology And Conceptual Solution Available
Level 3	Component And/Or Breadboard Validation In Laboratory Environment Exists
Level 4	Component And/Or Breadboard Validation In Relevant Ground Or Space Environment Completed
Level 5	System/Subsystem Prototype Demonstration In A Relevant Ground Or Space Environment Completed
Level 6	System Prototype Demonstration In A Space Environment
Level 7	Actual System Completed And "Flight Qualified" Through Test And Demonstration
Level 8	Actual System "Flight Proven" Through Successful Mission Operations

STEP 5: *Determine Schedule Requirements Necessary for Critical Questions (For each critical question identified in Step 2)*

Schedule Questionnaire

1. When is the information required? (Near-Term (i.e., Less than 5 years) =1, Mid-Term (i.e., 6 to 10 years) = 2, Far-Term (i.e., More than 10 years) = 3)
2. What is the research time and effort required? (Substantial =1, Moderate =2, Low = 3)
3. Is there a clearly defined sequential path of scientific investigations? (Yes =1, No = 2, Do Not Know at This Time = 3)
4. Are parallel or alternative pathways appropriate? (Yes =1, No =2, Do Not Know at This Time = 3)

APPENDIX A DESCRIPTION OF PROCESS

STEP 6: *Prioritization of Disciplinary Critical Questions*

All critical questions, from Step 2, have now been partitioned into five categories (i.e., Environmental Health and Life Support Systems, Countermeasure Systems, Medical Care Systems, Enabled Science and Basic Science). In addition, each question has been assigned one of four levels of criticality. Step 6 is a discussion and review of these findings to determine if specific items need to be recategorized or reprioritized.

- *Include additional critical questions from the Disciplinary Plans or as ad hoc inputs from the Executive Steering Committee resulting from these discussions, as necessary.*

STEP 7: *Implementation Strategies For Life Sciences - Matching Resources to Programmatic Options*

- *Include discussion of national and international cooperative activities including specific flight platforms, as necessary.*
- *Complete for each critical question identified in Step 2 and record responses on data sheet.*

(a) Discussion and Validation of Schedule and Requirements -

1. Discuss and validate the discipline groups inputs on the data sheets provided. The critical questions have been ordered with reference to time criticality (based on assessments in Steps 3, 4, and 5) within each criticality level (i.e., 1 through 4) for three of the five categories (i.e., Environmental Health and Life Support Systems, Countermeasure Systems, and Medical Care Systems).

(b) Platform Requirements -

1. What facilities are necessary to complete the activity (i.e., ground, Shuttle/Spacelab, SSF, robotic precursor missions, unmanned free-flyer, Moon outposts)? (*Record response by marking "X" in the appropriate column; provide comments if "other" columns or robotic precursors are selected.*)

2. Are flight validation studies required and in what sequence? (*Yes = 1, No = 2; if yes, provide written comments.*)

(c) Resource Requirements - People and Facility Needs

1. Are current ground facilities (NASA Centers, Universities and private Industry) sufficient to support the activity? (*Yes = 1, No = 2; if no, provide written comment on other facilities necessary to complete this activity*)

2. Is there a sufficient life sciences community of outstanding scientists committed or able to be recruited to support the activity? (*Yes = 1, No = 2*)

3. Will the activity serve as a vehicle for attracting new scientists into the NASA community? (*Yes = 1, No = 2*)

APPENDIX A DESCRIPTION OF PROCESS

(d) **Discipline Consolidation -**

Can this critical activity be grouped with any others from different disciplines?

- | | |
|---|--|
| <input type="checkbox"/> 1
<input type="checkbox"/> 2
<input type="checkbox"/> 3
<input type="checkbox"/> 4
<input type="checkbox"/> 5
<input type="checkbox"/> 6
<input type="checkbox"/> 7
<input type="checkbox"/> 8
<input type="checkbox"/> 9
<input type="checkbox"/> 10
<input type="checkbox"/> 11
<input type="checkbox"/> 12
<input type="checkbox"/> 13
<input type="checkbox"/> 14 | No - Can Not Be Grouped
Do Not Know At This Time
If Yes, Specify Discipline(s) and Provide Comments
Behavior, Performance and Human Factors
Regulatory Physiology
Cardiopulmonary
Environmental Health
Musculoskeletal
Neurosciences
Radiation Health
Cell and Developmental Biology
Plant Biology
Life Support, including CELSS
Planetary Protection
Exobiology |
|---|--|

STEP 8: ***Committee Products and Recommendations.** The Committee is repartitioned into groups representing the categories (i.e., Environmental Health and Life Support Systems, Countermeasure Systems, Medical Care Systems, Enabled and Basic Science).*

1. Develop a White Paper for each category and include recommendations and priorities for constrained and robust life sciences programs:

AEROSPACE MEDICINE ADVISORY COMMITTEE³

GOAL - To recommend an integrated Life Sciences research strategy for human exploration missions.

PRODUCT - Organize critical research or technology development questions into explainable, defensible, executable areas of focus and include consideration of optimum sequence.

STEP 1 For each critical question determine whether the SSF centrifuge can be used to resolve the issue. If the centrifuge is required, indicate by placing an "X" in the appropriate column on the data sheet.

STEP 2 Review data and develop draft report for Life Sciences strategic considerations for human exploration missions.

Footnote 3. Aerospace Medicine Advisory Committee (AMAC) — A NASA Advisory Council committee that reviewed, and in some cases, revised and reprioritized critical questions to generate this report. See Appendices A & B for details of membership and process.

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APPENDIX C AMAC CHARTER FOR THIS REPORT

The Aerospace Medicine Advisory Committee (AMAC) is charged to develop an implementation strategy in support of human Mars exploration missions. This plan will identify specific projects and areas of research, both basic and applied, within NASA and in collaboration with other government agencies and countries which will contribute to these objectives.

In view of the tight fiscal constraints facing NASA and OSSA in the out-years, the plan should prioritize the research needs on spacelabs and SSF in order to support advanced human space flight missions. This process should include a review and prioritization of the projects, research hardware and other laboratory facilities which will be necessary to carry out this research in a phased and timely manner.

In developing the plan the Space Life Science Division 1991 Strategic Plan should be reviewed. Inputs from other advisory committees should also be obtained. Specifically include participation of the Life Sciences Advisory Subcommittee of the Space Science and Applications Advisory Committee as well as the National Academy of Science Committee on Space Biology and Medicine and other advisory committees as appropriate. Participation from a wide ranging group representing experts from other government agencies and countries is encouraged.

On a final note, the plan should recommend a strategy which is consistent with the budgets and schedules for implementing the manned space flight goals mentioned above.

The plan should be available by mid January 1992 to serve as a basis for establishing the 1993 to 2005 mission planning and resources baseline.

APPENDIX D

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APPENDIX H

Requirements for Ground-Based and Flight Programs

Appendix H-1 Environmental Health and Life Support Systems

Quest#	Critical Question	1	2	3	4	5	6	7
1c1	What are the requirements for adequate quality of life as they relate to food, clothing, hygiene, vibroacoustics, lighting, and other personal needs (privacy, recreation) in spacecraft and habitats?	X	X	X			X	
1d2	What factors should be considered (e.g. maintainability, reliability, operator discretion) when allocating functions between humans and machines?	X	X	X			X	
1e1	What are the behavioral correlates of physiological changes induced by the space environment?		X	X			X	
2a3	What are the optimal environmental conditions for ensuring synchronization of circadian rhythms in space, and what are the most appropriate work-rest schedules for ensuring optimal health and performance?	X	X	X				
2f12	What are the effects of pressure and gas composition in space flight and during EVA on changes on fluid and electrolyte regulation?	X	X	X				
2g3	What environmental conditions of space flight influence temperature regulation?		X	X	X			
4a1	What impact do space flight-induced biological, physiological, and immunological changes have on the susceptibility of crewmembers to toxic materials alone or in combination? The concern is for both in-flight performance and residual health. (See Regulatory Physiology Discipline Science Plan 1991 for further discussion of immunological issues)		X	X	X			X
4a2	How can traditional limited-time exposure and human toxicological data be used to predict acceptable values for inhalation and ingestion exposures to single chemicals and/or to mixtures including biological toxins and particles under flight conditions?	X	X	X			X	
4a5	What are the potential biomarkers for assessing either exposure or response to chemicals?	X		X	X		X	
4a6	What are the effects of chronic exposure to ultrafine and larger (respirable and nonrespirable) particles on crew health, safety, and performance?	X	X	X			X	
4a7	What approaches may be used when insufficient data are available to allow prediction of acceptable exposure levels?	X						
4b1	What are the acceptable numbers and kinds of microorganisms in air, water, food, and surfaces?	X	X	X			X	
4b2	What is the effect of space flight on all microorganisms?	X	X	X	X		X	X
4b4	What technology is available to identify microorganisms in crew and environmental (air, water, surfaces) specimens. How are microorganisms controlled by anti-microbial procedures?	X	X	X			X	
4c1	What, if any, are the interactions between the effects of microgravity on crewmembers and the effects of off-baseline levels of atmospheric parameters, including gas composition, pressure, and temperature?	X		X			X	
4c5	What are the effects of all potential atmospheric components, including contaminants and factors on physical and psychological well-being and crew performance?	X	X	X			X	
5c12	What are the appropriate light wave length cycles to maximize vitamin D production?	X	X	X				
7a1	For a given mission, what are the fluxes of GCR in interplanetary space as a function of particle energy, LET, and solar cycle?							

1= Ground-based Research 2= Spacelabs 3= Space Station Freedom 4= SSF Centrifuge Facility
5= Robotic Precursor Missions 6= Lunar Base 7= Free Flyers (biosatellites)

Appendix H-1 Environmental Health and Life Support Systems

Quest#	Critical Question	1	2	3	4	5	6	7
7a2	What is the solar cycle dependence of space radiation?							
7a3	What is the trapped radiation flux as a function of time, magnetic field coordinates and geographical coordinates?	X						
7a4	What are the maximum flux, the integrated fluence, and the probability of large Solar Particle Events (SPE) during any mission?							
7a6	What are the doses related to heavy ions in deep space?							
7a7	What are the factors that determine radiation flux of solar flares?		X	X		X	X	X
7a8	What will the radiation environment be within the space vehicle and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?		X	X		X	X	X
7a9	How can protection against the effects of galactic cosmic rays and the proton radiation of solar events be improved?	X	X	X		X	X	X
7b1	What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?	X						
7b2	What are the angular distributions of nuclear interaction products?	X						
7b3	What are the particle multiplicities of nuclear interaction products?	X						
7b4	How is a radiation field transformed as a function of depth in different materials?	X						
7b5	What are the optimal ways of calculating the transport of radiation through materials?	X						
7c1	What is the precise energy deposition of heavy ions?	X						
7c2	What are the yields and energy spectra of electrons?	X						
7c3	How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?	X						
7c4	How do diffusion, recombination and other interactions of chemical intermediaries alter the chemical events at the DNA level?	X						
7c5	How is physical energy deposition related to biological effect?	X						
7d1	What are the probabilities of GCR to produce radiation damage at specific sites on DNA?	X						
7d2	How are processes like oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?	X						
7d3	What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, etc.)?	X						
7d4	How can molecular mechanisms of radiation damage be used to understand effects in whole cells?	X						
7e3	What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?	X						
7e4	How do cellular repair mechanisms modulate damage produced by energetic charged particles?	X						
7e5	How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?	X						

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Appendix H-1

Appendix H-1 Environmental Health and Life Support Systems

Quest#	Critical Question	1	2	3	4	5	6	7
7e6	How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?	X						
7f1	How can animal models be used to extrapolate probabilities of radiation risk to humans in space?	X						X
7f3	What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer; cataracts?	X						
7f5	What is the age dependence of relevant radiation effects in animals (cancer, cataractogenesis, life shortening, etc.)?							
7g1	What should be the radiation dose limits for manned deep space missions?	X						
7g3	What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure? What is the effect of GCR at different stages of the carcinogenesis process?	X						
7g4	What is the probability of cataract formation as a function of the same quantities?	X						
7g5	What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?	X		X	X			
8la4	What are the thresholds required for gravity to have an effect?	X	X	X	X			
8la6	What are the differences, if any, between species and their tissues in their perception and responses to gravity?	X	X	X	X			
8lb1	Can plants successfully reproduce through more than one generation in space?	X	X	X	X			
8lb2	Is chromosomal integrity and behavior during cell division affected in microgravity?	X	X	X	X			X
8lb3	Is cell, tissue, or organ differentiation affected in microgravity?	X	X	X	X			
8lb4	What effect does microgravity have on embryogenesis and the ensuing stages of the life cycle of plants from maturity to flowering and senescence?	X	X	X	X			
8lb5	Are microgravity-grown tissues and organs competent?	X	X	X	X			X
8lb6	Are the growth rates of higher plants or single cells affected by microgravity?	X	X	X	X			
8lb8	Are there unique interactions between space radiation (or other environmental factors) and microgravity that affect the development of biological systems in space?	X	X	X	X	X	X	X
8lc1	Are anabolic and catabolic pathways and the photosynthetic apparatus and pathway altered in microgravity?	X	X	X	X			
8lc2	What effect does microgravity have on the synthesis of storage and support polymers?	X	X	X	X			
8lc4	Are pathways for plant nutrient absorption altered in microgravity?	X	X	X	X			
8lc5	What are the effects of the space environment on long distance transport of water and on transpiration?	X	X	X	X			
8llc1	How is the effect of gravity (and microgravity) on cells influenced by magnetic fields and radiation?	X	X	X	X	X	X	X

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Appendix H-1 Environmental Health and Life Support Systems

Quest#	Critical Question	1	2	3	4	5	6	7
8Va1	What is the role of gravity in the regulation of circadian rhythms? — What are the effects of the absence of gravity on the generation, expression (period, phase, amplitude and/or waveform) and entrainment of circadian rhythms? — Is it at the synchronizing agent (zeitgeber)? — If not, is it necessary for the action of other synchronizing agents (light, exercise)? — What is the role of gravity in the ontogeny of circadian rhythms? — Is there a difference in the role of gravity across the phylogenetic scale? Single cells to complex organisms? — What is the gravity threshold for its actions in the regulation of circadian rhythms? Does this gravity threshold vary with the complexity of the organism?	X	X	X	X			
9a1	Can crop plants produce sufficient edible biomass extra-terrestrially to support human crews? The following constraints should be considered in studying this question: — Closed environments — Recycling — Limited space — Gravity effects — Phytochemical volatile compounds and other trace contaminants — Radiation — Adventitious biota (microbial and other)	X	X	X	X		X	X
9a3	What conditions are required to optimize the food generating and water recycling capacity of crop plants? The following factors represent the minimum that should be considered in studying this question: — Light quantity, quality, periodicity, gas composition and density — Root environment: substrate, nutrients, volume, temperature, etc. — Aerial environment: gas composition and pressure, temperature, planting density, etc.	X	X	X	X		X	
9a4	What are the effects of adventitious biota (microbial and other) over long periods in a CELSS?	X	X	X			X	
9a5	What robotic and automated procedures should be developed for planting, growing, and harvesting of crop plants?	X	X	X			X	
9a6	How can molecular genetic technology, including germplasm screening, be used to develop crop cultivars better fit for CELSS use in space? (for example) — Improve nutrient quality and bioavailability — Reduce natural toxicants — Optimize plant architecture	X	X	X			X	

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Appendix H-1

Appendix H-1 Environmental Health and Life Support Systems

Quest#	Critical Question	1	2	3	4	5	6	7
9a7	What is the potential for using the following alternative food sources in a CELSS? <ul style="list-style-type: none"> — Animals (aquatic and terrestrial, vertebrate and invertebrate) — Algae — Fungi — Bacteria — Non-traditional higher plants — Tissue-cultured cells — Synthetics 	X	X	X			X	
9b8	What are the specific nutritional requirements for humans in space? This question should consider at least the following: <ul style="list-style-type: none"> — Caloric requirements — Will the nutritional requirements of the crew change and require modified diets over time of flight — Fluid requirements — Distribution of the macro nutrients (protein, carbohydrate, lipid) — Fiber and micronutrient requirements 	X	X	X			X	
9b9	What are the acceptability criteria for foods and in what priority order should they be evaluated? Some criteria include: <ul style="list-style-type: none"> — Safety and freedom from toxic substances and infectious agents — How will the crew respond to diet on a Mars mission — Nutrient and attribute balance — Familiarity/cultural experience — Taste/texture/color/shape — Flexibility in preparation methods — Cooking (time, complexity, etc.) — Seasoning (diversity of options) — Compatibility with other menu items — Variety What food groups fulfill these requirements? <ul style="list-style-type: none"> — How can the biomass candidates be used or modified to achieve the desired requirements? 	X	X	X			X	

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Quest#	Critical Question	1	2	3	4	5	6	7
9b11	How stable in storage are foods considered for Mars mission and how can storage stability in space be increased? — What are the safety and quality considerations of storage? — What processes are feasible to use in a CELSS? — Are additives needed? If so, which ones? — What are the storage/inventory requirements? — For what types of foods will storage be unnecessary? — Is there a need for packaging? If so, which products will require it?	X		X			X	
9b12	What food processing and storage technologies will need to be developed for space application? — How will existing and new processing and storage techniques perform in the constraints of a CELSS environment? — What differences are there in product development for space compared to land-based activities? — What are the influences of processing, cooking, and serving on — nutrient and attribute stability? — How can processing and cooking techniques be used to modify and improve the acceptability of foods offered the crew?	X		X			X	
9b13	Can edible foods and/or ingredients be derived from non-edible plant wastes? — What are the crop plant-specific limits of this capability?	X		X			X	
9b14	How will non-recyclable materials be minimized in a CELSS program?	X						
9b165	How do the above nutritional questions apply to CELSS produced foods, used either as a nearly complete diet or as a supplement to stored food?	X		X			X	
9c168	What are the processing requirements necessary to handle human wastes? What are the health and safety requirements for the waste treatment subsystem?	X	EDC	X			X	
9c17	What are the processing requirements necessary to convert metabolic wastes into nutrients suitable for plant growth?	X		X			X	
9c18	What will be the limits of the composition of the processed waste streams with regard to the following parameters: — Organic an inorganic materials — Potentially toxic materials — Water content?	X						
9c19	What currently available waste treatment/nutrient regeneration technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application? (Note question 16.8)	X		X			X	
9c21	To what extent will micro-organisms used in a physico-chemical waste processor present an issue of performance degradation?	X	X	X			X	
9c22	What are the production rates and chemical compositions of the different waste streams that are to be processed in a CELSS?	X	X	X			X	
9c23	What can be done about food packaging, crop selection, etc., to minimize the amount of material that ends up in the waste streams?	X						

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Quest#	Critical Question	1	2	3	4	5	6	7
9c24	Can plant transpiration water qualify as potable and hygiene water? If not, what currently available water treatment technologies can be adapted to polish transpiration water in a CELSS, and what technologies will need to be developed for space application?	X		X			X	
9c245	What are the best technologies for recycling the water required for a Mars mission to acceptable potable and hygiene levels?	X	X	X			X	
9c25	If the crop plants in a CELSS can be used to meet the production rate demands for potable and hygiene water, then what types and numbers of plants will be required, and what environmental conditions will these plants require?	X	X	X			X	
9c26	What currently available water treatment technologies can be adapted to recycling the various grades of water (hygiene, wash, etc.) in a CELSS and what technologies will need to be developed for space application?	X	X	X			X	
9c27	What are the storage requirements for potable and hygiene water in a CELSS? Consider: — Safety/redundancy — Control of microbial film on surfaces — Volume	X	X	X			X	
9c28	What will be the acceptability thresholds for revitalized air in an operational CELSS?	X		X			X	
9c29	What currently available air treatment technologies can be adapted to a CELSS use, and what technologies will need to be developed for space application?	X	X	X			X	
9c30	What types and surface area of plants will be required to meet the production rate demands for revitalized air and what environmental conditions do these plants require?	X	X	X	X		X	
9d31	What strategies or techniques exist for monitoring and control of the known or suspected possible causes of life support system instability? Consider: — Pests or pathogens (disease) — SMACS — Toxicants produced by humans, by processing procedures, or by the plants themselves — Atmosphere leakage — Perturbations in environmental controls — Radiation — Microgravity — Unanticipated ecological interactions — Scheduled or unscheduled system or mission events — Failure of microbial cultures in algal fermentation systems — Food variety	X	X	X			X	

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Quest#	Critical Question	1	2	3	4	5	6	7
9d32	What are the requirements for CELSS system design and operation to achieve safe and reliable operation? Address the following: — Subsystem redundancy — Interaction with Chemical - Physical regeneration — System modeling and behavior — Alternative strategies for system monitoring and control — Failure of a subsystem	X		X			X	
9d33	Is a CELSS, because it operates within a limited volume and intense dynamics, subject to unknown or poorly characterized instabilities, such as chaotic behavior?	X		X			X	
9d34	What are the thresholds of system size (minimal) and system safety and reliability (maximal), and can these be extended in an integrated, controlled system?	X		X			X	
9d35	How can mathematical models be utilized to aid in system design, system simulation, and system operations?	X		X			X	
9d36	What are the power requirements and launch mass and volume for an operational CELSS ?	X		X			X	
9d37	What robotic and automated procedures should be developed for control, monitoring, and operations?	X		X			X	
9d38	What sensors are required for automation of a CELSS?	X		X	X		X	
9e39	What is the productivity, transpiration, and dry matter partitioning of plants at less than 1xg (micro-, 15%, and 38% gravity)?	X		X	X		X	
9e40	What is the morphology and reproductive capability of plants at less than 1xg (micro-, 15% and 38% gravity)? Will this modify crop selection criteria for space bases?	X	X	X	X		X	
9e41	What countermeasures can be utilized if productivity or reproduction is significantly decreased?	X	X	X			X	
9e425	Can the physico-chemical regenerative technologies and processes required for a Mars mission life support system function in the space environment? Consider: — Maintenance of liquid-gas interfaces (e.g., for nutrient delivery) — Transfers and separations of liquids, solids, and gases — Combustion What is the composition of air, water, and spacecraft systems and how is it monitored to assure crew health safety and performance?	X	X	X			X	
9e43	What are the effects of the space environment on microbial interactions with space systems and humans?	X	X	X			X	
9e44	Can proposed food processing techniques be modified to work effectively at reduced gravity?	X		X			X	
9f1a	Can safe and sufficient supplies of water and air be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of water and air for the Mars mission?							

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Quest#	Critical Question	1	2	3	4	5	6	7
9f1c	Can safe and sufficient supplies of food be provided for the trip/stay to/at Mars? Do current expendable systems exist to provide safe and sufficient supplies of food for the Mars mission?	X		X			X	
9f3a	Can wastes be successfully disposed of on a Mars mission without impacting planetary protection?	X		X			X	
9f4c	Do regenerative systems exist to provide safe and sufficient supplies of food for the Mars mission?	X		X			X	
9f5a	Do automated real-time systems exist to monitor air quality/toxicology for Mars mission?	X	X	X			X	
9f5f	Do automated systems exist to monitor food safety/quality for Mars mission?	X		X			X	
9f6a	Do systems exist to provide EVA/EHA capabilities required for Mars transit?	X	X	X				
9f6b	Do systems exist to provide EVA/EHA capabilities required for Mars surface exploration?	X					X	
10 1	What requirements should be placed on robotic and human missions (orbiters and landers) to protect Mars with respect to biological contamination imported from Earth (forward contamination)?	X		X		X	X	X
10 2	What provisions must be taken during the course of robotic and human exploration to protect the Earth from harm caused by the importation of biological materials from Mars (back contamination)?	X		X		X	X	X

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Appendix H-2 Countermeasure Systems

Quest#	Critical Question	1	2	3	4	5	6	7
1a3	What are the major human factors principles that govern optimal assignment of responsibilities between space crews and ground teams and among crew and team members? What ground-based organizations are required for effective support of flight crew performance on a Mars mission?	X	X	X			X	
1a4	What are the critical elements and processes involved in decision- making by ground teams and space crews operating autonomously or in combination?	X	X	X			X	
1a6	What are the critical characteristics of leaders that effect reciprocity and productivity of crews? What are the optimal crew command structures for a Mars mission?	X		X			X	
1a8	What are the optimal communication procedures for coordination among crew members and between ground and space crews?	X	X	X			X	
1a9	How does prolonged space flight affect behavior and group dynamics (including species, sex, and age differences)?	X	X	X	X		X	
1b1	What psychological and behavioral characteristics are exclusary? What behavioral and psychometric criteria should be used for selecting candidates for a Mars mission?	X		X			X	
1b2	What are the protocols for training effective ground teams and space crews in problem solving, enhanced communication, crew coordination, and interpersonal dynamics?	X	X	X			X	
1c2	What are the optimal designs for living/working areas in spacecraft/habitats to maximize morale and performance?	X		X			X	
1d1	What are the factors involved in integrating automated systems with human capabilities to promote productivity and reliability? What are the significant issues of control and intervention by human operators, and countermeasures for particular missions?	X	X	X		X	X	
1d3	What are the requirements for formatting, distributing, managing, accessing, updating, and presentation of information for optimal individual and crew performance? What are the requirements for crew input to the data management system?	X		X				
1d6	What are the human factors issues in teleoperation?	X	X	X		X	X	
1d7	What are the physical and cognisant performance capabilities and requirements of humans in different stages of space flight as a function of mission parameters, e.g. duration, gravity field, physical environment?	X	X	X			X	
1d8	What are the anthropometric requirements for work stations to accommodate individual team members to maximize performance?	X	X	X			X	
1d9	How can artificial intelligence systems be used to support human decision-making in long-duration space flight?	X		X			X	
1d10	What are the mission specific design and protocol requirements for telecommunications to optimize crew performance?	X	X	X			X	
1e2	What are the effects of living in the space flight environment on cognitive functions (including attention, memory, information processing and decision-making) and on work capacity?		X	X			X	
1e3	How do the fundamental behavioral processes of perception and sensation, learning and cognition, and motor skills change in space? What is the time course of adaptation?		X	X			X	

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Appendix H-2

Appendix H-2 Countermeasure Systems

Quest#	Critical Question	1	2	3	4	5	6	7
1f1	What procedures are needed for analyzing missions for their demands on human performance (e.g. task analytical techniques and models)?	X	X	X			X	
1f2	What are the most effective schedules for work, rest and recreation, exercise and sleep for enhancing human performance and adaptation during long-duration exposure to space?	X	X	X			X	
1f3	What are the special performance requirements and capabilities and equipment requirements for extravehicular activity (EVA)?	X	X	X			X	
1f6	How is workload optimized for various space explorations?	X	X	X			X	
1f7	What are the criteria for evaluating individual and crew performance and productivity during space missions of various durations?	X		X			X	
1f10	What minimally intrusive hardware and software capabilities are best suited for obtaining performance data in flight?	X	X	X			X	
1f11	How do circadian rhythm cycles and sleep influence performance and interact with the space environment to affect ability to accomplish mission goals? What countermeasures (e.g., pharmacology, lighting, etc.) can be developed to improve performance and productivity?	X	X	X	X		X	
1f13	What models can developed to describe the effects of fundamental behavioral stressors on mission performance?	X		X			X	
1f15	What are the best psychophysiological correlates of effective performance variation in the space environment? In what way do physiological changes incurred in space affect task performance?	X	X	X	X		X	
1g1	What are the effects of stress on crew and ground team performance and what method of detection and intervention strategies (e.g. selection, training, crew support) would prove effective?	X		X			X	
1g2	What methods characterize the process of individual and team adaptation to stressors (e.g. isolation, confinement, and risk) inherent in space flight?	X		X			X	
1g3	What are the factors that shape individual and team motivation and the ability to cope effectively with environmental stress?	X		X			X	
1g5	What are effective protocols for sustaining crews in case of loss of a crew member in flight, or loss of a family member or friend on earth?	X		X			X	
2a1	What are the effects of the space environment on sleep, sleep cycles, or the generation, expression (period, phase, amplitude and/or waveform), and entrainment of metabolic, endocrine, reproductive, and/or behavioral circadian rhythms? Of these effects, which result from altered gravity and which result from other environmental factors?	X	X	X	X		X	
2a2	What are the effects of intermittent and variable gravity fields on circadian rhythms, and how does this affect the use of artificial gravity as a countermeasure to microgravity?	X	X	X	X		X	X
2a6	What are the effects of exercise on circadian rhythms and sleep? What pharmacological and nonpharmacological (e.g. light, exercise) agents can be used to reset the human biological clock? What are the effects of routine administration of pharmacological agents in space on circadian rhythms and sleep?	X	X	X	X		X	

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Quest#	Critical Question	1	2	3	4	5	6	7
2a7	What are the appropriate ground-based analogs for studying the effects of extreme environments on human circadian rhythms?	X		X			X	
2a8	What are appropriate research models for simulating the effects of the space environment?	X						
2a9	What are the effects of non-gravity-related physical-chemical and psychological space-flight-induced stressors on circadian rhythms and sleep?	X	X	X	X		X	
2a11	What roles do age and gender play? Is there a response of the circadian system to the space environment?	X	X	X			X	
2a12	What are the effects of cephalad fluid shifts on circadian rhythms?	X	X	X	X		X	
2c1	Does the well documented decrease in red blood cell mass termed "anemia of space flight" represent a normal microgravity-associated adaptive process (self-limiting) or a transient response (self-correcting) to changes brought about by various space-flight-related stimuli (stressors)?	X	X	X	X			X
2c3	What is the most effective way to restore red cell mass during simulated and actual microgravity? Should red cell mass be restored during space flight? Are these acute or chronic changes and are they of sufficient magnitude or duration to pose an unacceptable medical risk and warrant the development of countermeasures (prophylactic or therapeutic)? Formulate mathematical and computer models of tissue adaptation and cellular transient response to altered load histories?	X	X	X	X			
2d5	What are the relationships between the stressors associated with space flight; the source, duration and magnitude of the stressor; and decreased immune function? — Are there effective operational procedures or countermeasures to counteract the stressors or their effects?	X	X	X			X	
2d6	Are there terrestrial (1 g) human, animal and/or computer models that simulate or reproduce the effects of space flight/microgravity with regard to the immune system in space?	X	X					
2e1	Is the basal metabolic rate and metabolic efficiency altered during extended space flight? Are there changes in energy metabolism and storage in space, especially in substrate utilization?	X	X	X	X			
2e2a	What are the effect of changes in cell and nutrient turnover during space flight on nutritional requirements?	X	X	X	X			
2e2b	What are the optimal noninvasive microanalytical methods and techniques for use during space flight to monitor nutritional status?	X	X					
2e3	What are the mechanisms underlying the negative nitrogen balance and changes in lean body mass incurred during space flight? What are the possible interventions, including dietary alterations in proteins and amino acids?	X	X	X	X		X	
2e5	Do the effects of space flight require added supplements of vitamins, minerals, or other nutrients? What is the safe range of exogenous vitamin intake for long-term space flight? Are nutritional requirements modified by transient digestive disturbances, such as the anorexia, nausea, and vomiting associated with space sickness?	X	X	X	X		X	
2e8	What is the time course and nature of body composition change due to space flight? Do changes in body composition (age and gender) have an effect on crew health and performance?	X	X	X	X		X	

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Appendix H-2 Countermeasure Systems

Quest#	Critical Question	1	2	3	4	5	6	7
2f2	What are the fluid and electrolyte regulating mechanisms underlying the cardiovascular responses to microgravity?	X	X	X	X		X	
2f3	What are the mechanisms for the chronic adaptive shifts in fluid and electrolytes during space flight? How does the new steady state affect the body's ability to respond to heat stress, electrolyte loading, EVA, and countermeasures?	X	X	X	X		X	
2f5	What are the best methods to accurately measure fluid loss, fluid intake, plasma volume, extracellular fluid, total body water, and interstitial volume in space flight?	X	X	X			X	
2f8	What are the effects of circadian rhythm changes in space flight on the responsiveness of the fluid and electrolyte system?	X	X	X	X		X	
2f10	What are the roles of renal blood supply and renal electrolyte handling in extracellular fluid volume control during simulated and actual microgravity?	X	X	X	X		X	
2g4	What are the effects of prescribed countermeasures on thermoregulation?	X	X	X	X		X	
3a1	Of the various countermeasures available to combat adverse cardiovascular effects on long- and short-duration missions, which are most effective, when and how should they be applied, and in what sequence? These include but are not limited to LBNP, fluid anti-g rehydration, centrifugation, and exercise.	X	X	X	X		X	X
3a2	What are the specific mechanisms underlying the orthostatic hypotension observed after flight? What are the effective countermeasures for this?	X	X	X	X		X	X
3a4	What is the relationship between the cardiovascular adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	X	X	X	X		X	X
3a5	Are the baroreflexes modified by space flight and how do these affect orthostatic tolerance? Are chemoreflexes and osmoreflexes modified by space flight and how do these affect orthostatic tolerance?	X	X	X			X	X
3a10	How are countermeasures to adverse cardiovascular effects of long- duration space flight affected by changes in fluid distribution?	X	X	X	X		X	X
3a11	Are there appropriate animal and/or computer models for studying each functional element of cardiovascular adjustments to microgravity?	X	X	X	X		X	
3a21	What is the relationship between cardiovascular response and exposure to varying gravity levels (force, internal frequency, and time interval)? Is there a threshold?	X		X	X		X	
3a26	Are there changes in cardiac performance and contractile efficiency during long term exposure to microgravity?	X	X	X	X			X
3b6	Is pulmonary function altered in long-duration space flight at rest, exercise, or in a disease state?	X	X	X	X		X	
3b7	Are there appropriate animal and/or computer models for studying each functional element of pulmonary adjustments to microgravity? What is the relationship, if any, between the pulmonary adjustments to space flight and those occurring in Earth-based models such as bedrest, immersion, and head-down tilt?	X	X	X	X		X	X

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Quest#	Critical Question	1	2	3	4	5	6	7
4c8	What are the adaptations and deteriorations associated with prolonged exposure to unusual atmospheric environments, including the impact of microgravity, and how can countermeasures be utilized against these deteriorations?	X	X	X			X	X
5a1	What is the time course and extent of muscle atrophy during either prolonged spaceflight or unloading?	X	X	X	X		X	
5a2	How is muscle metabolism regulated during normal activity and exercise, after acute and chronic unloaded states, and during recovery from unloading?	X	X	X	X		X	
5a4	What are the physiological similarities and differences of ground-based models of muscle atrophy and fiber transformation and weightlessness-induced muscle atrophy and fiber transformation? How valid are ground-based models for studying the characteristics of space-flight-induced muscle changes?	X	X	X	X		X	
5b1	What are the molecular signals and mechanisms that are responsible for the control of muscle hypertrophy and atrophy, and what are the specific stimuli that are generated by exercise or disuse to signal increased or decreased protein accumulation in muscle cells?	X	X	X	X		X	
5b2	What is the molecular interrelationship between catabolic and synthetic rates of protein metabolism in unloaded muscles?	X	X	X	X		X	
5b3	What are the effects of altered levels of hormones and their receptors in regulating the physiology of unloaded muscle?	X	X	X	X		X	
5b4	What is the link between mechanical activity (stress) and hormonal state in regulating protein turnover and gene expression and structure and function of muscle, as investigated by both ground-based and flight experiments? How can this information be used to integrate neuromuscular and musculoskeletal models of mechanics and adaptation to develop countermeasure protocols?	X	X	X	X		X	
5b5	What is the role of specific hormones, pharmacologic agents, and growth factors in regulating protein and gene expression in response to unloading?	X	X	X	X		X	X
5b6	What are the effects of unloading on the muscular intracellular and extracellular matrix?	X	X	X	X		X	
5b7	What is the molecular basis for the effects of unloading on the susceptibility of muscle to injury or damage upon resuming normal weight-bearing states?	X	X	X	X		X	
5c1	What are the rate, extent, and time course of bone and connective tissue loss for different areas of the body during exposure to microgravity or simulated microgravity? How is the time course of regional tissue loss correlated with changes in the tissue stress and strain histories at the same site? To changes in regional microcirculation? To other regional and systemic factors?	X	X	X	X		X	
5c2	Which endocrine and nutritional processes are required for maintenance of bone and connective tissue? How do these processes interact with mechanical loading? Are these processes affected by space-flight?	X	X	X	X		X	
5c3	What are specific countermeasures that impact effectively upon bone and connective tissue structure and function?	X	X	X	X		X	
5c5	What are the similarities and differences of ground-based models and spaceflight-induced bone and connective tissue loss with respect to biomechanical, histomorphometric, biochemical, and hormonal changes?	X	X	X	X		X	

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Quest#	Critical Question	1	2	3	4	5	6	7
5c6	Is bone loss reversible in terms of mass, ultra- and micro-structural organization, and microstructure? To what extent do irreversible architectural adaptations affect structural integrity?	X	X	X	X		X	
5c7	What are histomorphological and architectural changes that occur in bone and connective tissue because of space-flight?	X	X	X	X		X	
5c8	How does mechanical stress and changes in stress contribute to bone and connective tissue formation? Are stress and/or changes in stress required for continued structural integrity?	X	X	X	X		X	X
5c9	What are the critical characteristics or components of normal daily tissue stress and strain histories that regulate bone and connective tissue development, maintenance, and adaptation? How are these characteristics affected by microgravity?	X	X	X	X			X
5c10	How are regional changes in bone and connective tissue related to regional changes in muscle tissue?	X	X	X	X			X
5c11	How are neuromuscular activation patterns and musculoskeletal mechanics altered during activity (including exercise) in microgravity compared to 1-g?	X	X	X	X			X
5d1	What are the patterns of in-vivo mechanical loading (e.g., tissue strain, stress, strain rate, stress rate) in normal and low-g environments?	X	X	X	X		X	
5d3	What are the bone and connective tissue markers of metabolism (protein synthesis, secretion, and degradation)? How can bone marker data be used to investigate and predict regional changes in bone metabolism?	X	X	X	X		X	
5d4	Which endocrine-receptor perturbations modulate tissue responsiveness to mechanical stresses?	X	X	X	X		X	
5d5	Which specific models predict bone and connective tissue structural transients during altered load environments?	X	X	X	X		X	X
5d6	What key elements of bone and connective tissue structural assembly impact the biomechanical properties?	X	X	X	X		X	
5d7	Are there specific load histories that affect the macromolecular assembly of connective tissues?	X	X	X	X		X	X
5d8	What are specific signal transduction processes relevant to the modulation of structural molecules during altered load histories?	X		X	X			
5d9	How do changes in mechanical forces and tissue stress (e.g., shear, stress) and/or electrical forces (piezoelectric and tissue streaming potentials) result in mechanisms that are associated with translational alterations in connective tissue structural proteins?	X		X	X			
5d10	Is cytokine production and response to cytokine by osteoblasts and osteoclasts affected by exposure to microgravity?	X	X	X	X		X	X
5d11	Are precursor cells of osteoblasts and osteoclasts affected by microgravity?	X	X	X	X		X	X
5d12	Do precursor bone cells respond to maturation stimuli in a microgravity environment as they do on earth?	X	X	X	X		X	X
5d13	Do osteoblast require gravity to function normally? If developed in microgravity will they function normally?	X	X	X	X		X	X
6a1	Are there changes in the processing of signals from the semicircular canals or otolith organs that occur with adaptation? Do these changes take place within the vestibular nuclei, cerebellar structures or other related brainstem and cortical structures? What is the time course of such changes and do they correlate with space motion sickness?	X	X	X	X		X	X

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Quest#	Critical Question	1	2	3	4	5	6	7
6a2a	What are the circuitry and signals in the vestibular nuclei and brainstem that generate a gravito-inertial frame of reference? What are the roles of the different regions of the cerebellum?	X	X	X	X		X	X
6a3	What are the neural (morphophysiological) and neuroendocrine bases for motion sickness? What changes in neurotransmitters, neuroendocrine, or neurohumoral release can be correlated with space motion sickness?	X	X	X	X		X	X
6a6	What is the distribution of receptors for anti-motion sickness drugs in central vestibular pathways?	X	X	X	X		X	X
6b1a	How does gaze stabilization change in altered gravitational states? What are the characteristics of gaze and eye-head coordination with varying visual, vestibular, and somatosensory inputs?	X	X	X			X	X
6b1b	What is the most appropriate three-dimensional model of the angular and linear VOR and of central vestibular processing that will account for alterations in eye movements in microgravity?	X	X	X			X	X
6b2	What are sensory inputs and coordination of muscular outcomes organized for generation of posture and locomotion before, during, and after flight?	X	X	X	X		X	X
6b3	What are the optimal countermeasures for motor readaptation to partial-g or 1-g after adaptation to microgravity?	X	X	X	X		X	X
6b4	What are the pharmacology, physiology, and output pathways that control the autonomic and endocrine outputs characteristic of motion sickness?	X	X	X	X		X	X
6b5	What adaptive processes modify motor control systems? What is the dynamic range of adaptation of motor responses in altered states of gravity?	X	X	X	X		X	
6b7	What models of sensory-motor transformation can be used to predict motor behavior best in altered gravitational states?	X	X	X	X		X	X
6c2a	What psychophysical correlates can best be used to describe spatial orientation?	X	X	X			X	X
6c3	Does a change in vestibular input lead to changes in visual and auditory localization and multisensory spatial orientation?	X	X	X			X	X
6c4	What ground-based paradigms and models are most effective in evaluating interactions of angular and linear acceleration, proprioception, somatosensory and visual inputs in determining orientation in a three-dimensional environment? How do these interactions change in altered gravity?	X	X	X	X		X	X
6c5	What processes explain the altered perceptions of joint and body position in microgravity?	X	X	X			X	X
6e1	Will the decrease in afferent input to the vestibular, proprioceptive and somato-sensory systems associated with long-duration flights result in permanent reflex deficits?	X	X	X	X		X	X
6e2	If an on-board centrifuge is used as a countermeasure (physiological system maintenance), will going from 1-g to microgravity cause repeated maladaptions?	X		X	X		X	
7g7	What pharmacological agents should be developed and tested as prophylactic agents for low LET?	X	X				X	X

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Appendix H-2 Countermeasure Systems

Quest#	Critical Question	1	2	3	4	5	6	7
8IIb3	How are the following cell functions influenced by gravity and/or affected by microgravity: the expression and regulation of genetic information; cell division; cell differentiation; signal transduction, including signal-membrane interactions, membrane-effector interactions, and signal-effector linkage; membrane dynamics; intracellular transport; secretion; alternate pathway regulation; and cell-to-cell communication? The importance of selecting cells and cell lines that can provide interpretable results bearing on precise questions cannot be overemphasized.	X	X	X	X		X	X
8IIb5	How will altered gravitational fields and vectors change the information content of the three-dimensional microenvironment of the cells (stroma and matrix connections)? How does microgravity affect these signals under both homeostasis and challenge? Representative challenges would be wounding of dermal fibroblasts and keratinocytes (or epidermal/dermal wounding in vivo), differentiation of microvessel endothelial cells in vitro (or growth of the microvasculature in vivo, particularly following wounding or tumor implantation), and application of stress to active osteoblasts (or bones in vivo).	X	X	X	X			X
8IIb8	How long can single cells cope with changes in gravitational force without adverse results? Do these effects persist after return to unit gravity?	X	X	X	X		X	X
8III8	What structural and morphometric alterations will occur in the extracellular matrix, the connective tissue, and the musculoskeletal systems in long term spaceflight? — How will this result in altered differentiation of cells, and in changed tissue composition?	X	X	X	X		X	
8III13	What are the joint effects of radiation and microgravity? — How do neoplasms common to chronological aging relate to limitation of cell lifespan and susceptibility to abnormal growth regulation under altered gravitational fields?	X	X	X	X		X	X
8IVb1	What are the subcellular mechanisms whereby hair cells transduce acceleratory information, amplify it and bring about signal transmission? Is there a fundamental mechanism that is true across the animal kingdom?	X	X	X	X		X	X
8Vb1	How does gravity affect the regulation of metabolism,? Basal metabolic rate? Energy, metabolism, storage and substrate utilization? Body composition (fat and protein metabolism)?	X	X	X	X		X	X
8Vb2	What is the role of gravity in the regulation of the distribution, composition, and pressure of water/fluids in living systems from cells to complex organisms? How do these changes influence other homeostatic and regulatory mechanisms?	X	X	X	X		X	X
8Vb4	How does microgravity affect the function including feeding behaviors of gastrointestinal function?	X	X	X	X		X	
8Vb5	What is the role of gravity on sensory thresholds (audition, visual, taste, pain)? How do endocrine, neurohumoral, and metabolic mechanisms influence this effect?	X	X	X	X		X	
8Vb7	What role do endocrine and neural systems play in controlling/modifying adaptation to gravity?	X	X	X	X		X	
8Vb10	How does gravity interact with other environmental factors to control regulatory physiology and behavior?	X	X	X	X		X	X

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Appendix H-2 Countermeasure Systems

Quest#	Critical Question	1	2	3	4	5	6	7
8VI1	Is musculoskeletal growth, development, and function compromised during spaceflight and can they readapt upon return to Earth? The structure and functional systems that should be examined carefully are: (1) the postural muscles, (2) muscle spindles, (3) weight/load-bearing bones and joints, (4) intervertebral discs, (5) the architecture of the connective tissues of the body and (6) musculoskeletal innervation.	X	X	X	X		X	X
8VI2	What are the systemic, local, cellular, and subcellular mechanisms involved in adaptation to altered gravity especially bioenergetics and associated processes and cell-to-cell interactions?	X	X	X	X		X	X
8VI4	What is the role of fluid redistribution in the response of the musculoskeletal system to altered gravity and how does gravity impact the homeostasis of fluid compartments within tissues?	X	X	X	X		X	X
8VI6	What are the biochemical pathways responsible for synthesis, secretion, assembly, distribution, and degradation of structural and functional proteins in muscle in response to altered gravity?	X	X	X	X		X	
8VI7	What are the transduction mechanisms that couple mechanical stress to musculoskeletal mass and strength? What are the activation and force development processes of muscle and bone cells?	X	X	X	X		X	
8VI9	What signals the musculoskeletal adaptation to spaceflight? Are the signals the same as those found in biomechanical unloading on Earth?	X	X	X	X		X	
8VI10	What local changes occur in the musculoskeletal system in response to changes in stresses, strains, and strain rates?	X	X	X	X		X	X
8VI15	Do various risk factors(e.g., age, gender, species, strain (race), nutrition) modulate the musculoskeletal response to altered gravity?	X	X	X	X		X	X
12 1	Do we need artificial gravity countermeasures to protect from physiological deconditioning of a mission to Mars?	X	X	X	X		X	X
12 2	How should artificial gravity be applied in terms of g-load, rotation rate, and intermittent versus continuous exposure?	X	X	X	X		X	X

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Appendix H-3 Medical Care Systems

Quest#	Critical Question	1	2	3	4	5	6	7
2b1	What are the effects of space-induced endocrine changes on the function of other homeostatic systems (e.g. cardiovascular, central nervous system, immune function, thermoregulation, reproductive system, gastrointestinal system, and energy metabolism)?	X	X	X	X		X	X
2d3	Are there in-vitro tests that reliably predict decreases in immune function in space flight?	X	X	X	X			
2d4	What are the long-term effects of prolonged space flight after return to 1 g?	X						
2d9	How long do neutrophilia, lymphocytopenia, monocytopenia, eosinopenia, and reduced blastogenic responses persist after flight?	X	X	X	X		X	
2e4	What are the pharmacokinetics (absorption, distribution, metabolism, and elimination) of drugs likely to be used in space? Which methods of administering drugs are the most effective in providing a predictable response during space flight?	X	X	X	X		X	
2e11	Does space flight alter gastrointestinal function, including the absorption of essential nutrients and the functioning of gut flora? What are the effects of space flight on liver function? Are the effects progressive? Are they reversible?	X	X	X	X		X	
2e14	What is the nature of space flight-induced changes in effect of vasoactive drugs?	X	X	X	X		X	
2e15	What is the nature of space flight-induced effect of pharmacokinetics of drugs?	X	X	X	X		X	
2f1	What are the time course and magnitude of fluid shifts and changes in fluid compartment volumes during acclimatization to hypogravity and during return to 1 g after flight?	X	X	X	X		X	
2f4	What are the effects of microgravity on renal function, e.g. stone risk? Are the effects progressive? Are they reversible? Are there differences in filtration, reabsorption, secretion, and excretion?	X	X	X	X		X	X
2f6	What are the time course and magnitude of the diuresis, natriuresis, and kaliuresis resulting from exposure to hypogravity?	X	X	X	X		X	
2g1	What are the effects of space flight and/or EVA on thermoregulation processes and heat exchange?	X	X	X	X			
3a3	What are the cardiovascular responses to extravehicular activity (EVA) at various levels of gravity (e.g., microgravity, planetary surface exploration)? What factors influence the occurrence, magnitude, and sequence of these responses?	X	X	X	X		X	
3a6	There is an increase in cardiac arrhythmias associated with space flight and, if so, what are the specific mechanisms responsible for them?	X	X	X			X	
3a9	Does the extent of adaptation affect postflight orthostatic tolerance?	X	X	X	X		X	
3a12	Following long-term space flight, are there delayed or persistent consequences, either beneficial or harmful? As a corollary, are there appropriate rehabilitative measures that should be applied both in the near-term (hours to days) and long-term (months to years) after flight?	X		X	X		X	
3a13	Since microgravity alters blood pressures and flows to some tissues, what are the structural and functional consequences in these various tissues and organ systems with long-duration flights?	X	X	X	X		X	

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Appendix H-3 Medical Care Systems

Quest#	Critical Question	1	2	3	4	5	6	7
3b2	In the environment of microgravity, does the absence of sedimentation cause deeper penetration by aerosol particles in the lung? In the spacecraft environment, what are the aerosol concentrations, particle size profiles, and bacterial contaminations? Do these factors constitute a health hazard?	X	X	X	X			
3b3	Which pulmonary life support procedures should be used for effective protection or resuscitation of crewmembers in the event of loss of pressure in the EVA suit or cabin, and for cardiopulmonary resuscitation and general anesthesia?	X	X	X			X	
4b3	What is the effect of long-duration space flights on the human immune system? (Reg. Physiol see p. 6)	X	X	X			X	
4c2	What procedures and approaches prevent decompression sickness or minimize crew risk?	X		X			X	
4c3	Treatment of medical problems of spacecraft inner temperature, and adverse effects of the gaseous environment?	X	X	X			X	
4c9	What are the risks for bubble formation and clinical decompression sickness associated with various pre-EVA denitrogenation/decompression schedules and exercise?	X	X	X			X	
5a9	Does the atrophy from unloading make muscle, tendon, and the myotendinous junction more susceptible to injury or damage on resuming normal weight-bearing states?	X	X	X	X		X	
5a10	How completely and how well does injured muscle repair in microgravity?	X	X	X	X		X	
5c4	What potential risks does bone loss present to the development of bone fractures, hypercalcemia, metastatic calcification, and renal stone formation?	X	X	X	X		X	
7g6	How are risks associated with acute exposure to space radiation to be managed medically?	X		X			X	
8III1	How will the reproductive status of premenopausal female crewmembers be managed to minimize the risk of pregnancy, osteoporosis, and hemorrhage from ruptured follicles during ovulation? What is the role of gravity in developmental biology? — Does the developmental ontogeny of animals raised through more than one life cycle under a changed gravity field differ from the 1-g classical pattern? Does this altered pattern reside in the genome, or is it relayed from hormonal and stromal interactions? — Are there critical windows of susceptibility for developmental processes, or is development affected in a gradient? — If gravity-related effects exist, can they be reversed in the short- or long-term? — What will be the result of gravity-induced dys-synchrony (temporal or hormonal) during development?	X		X	X			

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Appendix H-3 Medical Care Systems

Quest#	Critical Question	1	2	3	4	5	6	7
8III4	What are the effects on the male and female germ cells of protracted, chronic, low dose exposure to space radiation outside the Van Allen belts? What events in gametogenesis and early germ cell maturation are gravity sensitive, and how can these results relate to the proliferation and differentiation of other individual cell types? — Can altered gravities affect fertilization, and do these results indicate more general mechanisms of membrane alteration in individual cells? — Which responses are transmitted maternally, and which are intrinsic to the developing embryo? — What are the results of altered gravity fields on the axis polarity and symmetries of the zygote? — Are there gravity effects that can terminate in changes of gene activation?	X	X		X		X	X
8Vb3	What is the role of gravity on thirst and feeding behaviors (appetite, taste preference, and thresholds)?	X	X	X	X		X	X
8Vb9	How does gravity affect compensatory mechanisms (e.g. endocrine, organ, circulatory, regenerative processes)? What is the interaction with growth stages? What is gravity's effect on wound healing?	X	X	X	X		X	X

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APPENDIX I ACRONYM LISTING

Adapt	Adaptation
ADV	Advanced
AFT	Autogenic Feedback Training
AMAC	Aerospace Medicine Advisory Committee
AMWG	Aerospace Medicine Working Group
ARC	Ames Research Center
BMAC	Biomedical Monitoring and Countermeasures
CELSS	Controlled Ecological Life Support Systems
CFR	Code of Federal Regulations
CHeCS	Crew Health Care System
CHROMEX	Chromosome Experiment
CNES	Centre National of Etudes Spatiales
CNS	Central Nervous System
CS	Countermeasures Systems
CSA	Canadian Space Agency
CT	Computerized Tomography
CV	Cardiovascular
DARA	Deutsche Agentur Fur Raumfahrt Angelegenheiten
DEF	Definition
DELIV	Deliverables
Demo	Demonstration
DEV	Development
DMES	Dimethylethoxysilane
DOD	Department of Defense
DOE	Department of Energy
D.V.M	Doctor of Veterinary Medicine
DWG	Discipline Working Group
ECF	Exercise Countermeasure Facility
EDOMP	Extended Duration Orbiter Medical Program
e.g.,	For Example
EHA	Extra-Habitat Activities
EHLSS	Environmental Health and Life Support Systems
EHS	Environmental Health System
EMTC	Extended Man-Tended Capability
EPA	Environmental Protection Agency
ESA	European Space Agency
etc.	Et Cetera
EVA	Extra-Vehicular Activities
FAC	Facility
FDA	Food and Drug Administration
FY	Fiscal Year
g	Gravity
GCR	Galactic Cosmic Radiation
HDQ	Headquarters
HDT	Head Down Tilt
HEI	Human Exploration Initiative
HMF	Health Maintenance Facility
Hyp	Hypergravity
HZE	Heavy Charged Particle

APPENDIX I ACRONYM LISTING

	High Atomic Number, Z, and Energy, E, Particles
i.e.,	For Example
IML	International Microgravity Laboratory
IOC	Initial Operating Capability
	Initial Operational Capability
IPA	Initial Payload Analysis
JEM	Japanese Experiment Module
JSC	Johnson Space Center
K	Thousands
KSC	Kennedy Space Center
LABS	Laboratories
LBNP	Lower Body Negative Pressure
LDM	Long Duration Missions
LET	Linear Energy Transfer
LMEPO	Lunar, Mars Exploration Planning Office
M.D.	Medical Doctor
M.P.H.	Master of Public Health
M.S.	Master of Science
MCS	Medical Care Systems
Mech	Mechanics
MFPE	Mission From Planet Earth
MRI	Magnetic Resonance Imaging
MS	Musculoskeletal
MSRO	Mars Site Reconnaissance Orbiters
MSVR	Mars Surface Rovers
MTC	Man-Tended Capability
MTPE	Mission To Planet Earth
NASA	National Aeronautics and Space Administration
NASDA	National Space Development Agency of Japan
Neurolab	Neurological Laboratory
Neuroscience	Neurological Science
NIH	National Institutes of Health
NMR	Nuclear Magnetic Resonance
NOAA	National Oceanographic and Atmospheric Administration
NOC	Next Operating Capability
NRC	National Research Council
NS	Neurosensory
NSCORT	NASA Specialized Center of Research and Training
NSF	National Science Foundation
NSTS	National Space Transportation System
O ₂	Oxygen
OAST	Office of Aeronautics and Space Technology
OPS	Operations
OSSA	Office of Space Science and Applications
p	Page
PC	Physico-Chemical
Perf	Performance
Ph.D.	Doctor of Philosophy
Physiol	Physiology

APPENDIX I ACRONYM LISTING

PIs	Principal Investigators
PMC	Permanently Man-tended Capability
Psych	Psychological
Reg	Regulatory
REPT	Report
REQ	Requirements
REQTS	Requirements
RES	Research
Resp	Response
Ret	Retired
RTOP	Research and Technology Operating Plan
SBI	Space Biology Initiative
SCI	Science
	Sciences
Secr	Secretion
SEI	Space Exploration Initiative
SETI	Search for Extraterrestrial Intelligence
Sim	Simulated
Skylab	Sky Laboratory
SL-J	Space Laboratory-Japan
SLS	Space Life Sciences
SMAC	Spacecraft Maximum Allowable Concentration
Spacelabs	Space Laboratories
SPE	Solar Particular Events
SSF	Space Station Freedom
TBD	To Be Determined
Tech	Technical
TECH	Technology
U.S.	United States
U.S.S.R.	United Soviet Socialist Republics
Univ.	University
US	United States
USAF	United States Air Force
USDA	United States Department of Agriculture
vs	Versus
μg	Microgravity
<	Less Than
>	Greater Than

